Quarterly Review of

INTERNAL MEDICINE AND DERMATOLOGY

VOLUME 8 NO. 3 SEPTEMBER 1951

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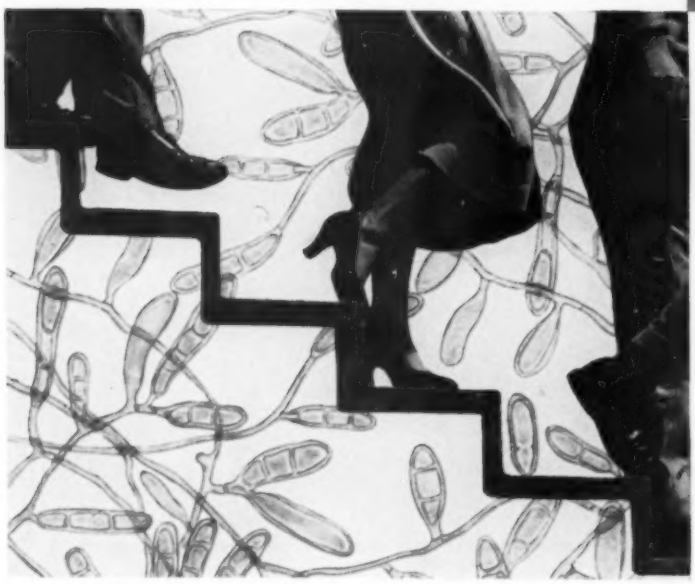

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1. Peck, S. M., and Russ, W. R.: Arch. Dermat. & Syph. *56*:601, 1947.
2. Nettleship, A.: Arch. Dermat. & Syph. *61*:669, 1950.
3. Brewer, W. C.: Arch. Dermat. & Syph. *61*:681, 1950.

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INCORPORATING THE INTERNATIONAL RECORD OF INTERNAL MEDICINE AND DERMATOLOGY

FOREWORD

The QUARTERLY REVIEW OF INTERNAL MEDICINE AND DERMATOLOGY provides a systematic and selective system for bringing together, in one publication, a quarterly summation of the clinical and experimental developments in internal medicine and the related medical specialties on a world-wide basis. During the past several years, eminent teachers and clinicians have given much thought and effort as to the best bases for selection and the most practical methods for classifying these data for quick clinical reference and easy collateral reading. Through this cooperative effort there has been developed in the QUARTERLY REVIEW an assured system for definitely keeping abreast of the currently approved new therapeutic procedures and opinions based upon the consensus of internationally recognized authorities. This plan not only saves time and expense but also through the annual cumulative index builds, for each subscriber, a permanent reference work unsurpassed for scope and authority. Emphasis is placed upon the clinical application of the newer therapeutic agents and procedures; therefore, specific dosages are given, reactions and contraindications are discussed, and all other essential data are presented so that these newer methods may be promptly, safely, and successfully applied by all who refer to the QUARTERLY REVIEW. For quick reference and to facilitate the uses of these data for collateral reading the following classifications are employed:

MEDICINE

Infectious Diseases
Chemotherapy of Infectious Diseases
Diseases Caused by Animal Parasites
Respiratory Disorders and Diseases
Cardiovascular Disorders and Diseases
Genitourinary Disorders and Diseases
Gastrointestinal Disorders and Diseases
Blood and Lymphatic Disorders and Diseases
Allergic Disorders and Diseases
Deficiency Diseases and Metabolic Disorders
Nervous and Muscular Disorders and Diseases
Miscellaneous

DERMATOLOGY

SYPHILOLOGY

BOOK REVIEWS

NEWS, NOTES, AND COMMENTS

A section entitled International Record of Internal Medicine and Dermatology is to be included at the beginning of the journal. This Record Section will consist of advanced experimental and clinical reports.

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internal medicine

INFECTIOUS DISEASES

Histoplasmin and Coccidioidin Sensitivity in Norway. J. BOE, V. LINDEN, AND J. TVEIT, Bergen, Norwak. Acta med. Scandinav. *139*:196-202, f.1, 1951.

The authors have examined a total of 1,074 persons with reference to histoplasmin and coccidioidin sensitivity. Most of them were patients in medical and surgical wards, and some of them doctors, medical students, and nurses. Altogether 27 persons reacted to histoplasmin alone, and 3 to coccidioidin alone (one of them had lived in California). There were 23 persons who reacted to both histoplasmin and coccidioidin.

None of the positive reactors showed any sign of pulmonary disease or other disease which could be connected with a mycotic infection. As practically all the persons tested were tuberculin-positive, any examination for pulmonary calcification was not likely to be instructive. But there are reasons for believing that some of the positive reactions to histoplasmin were caused by past or present infections with *Histoplasma capsulatum*.

The relatively large number of persons giving a positive reaction to both antigens indicates that in these cases the reactions must be regarded as cross reactions due to systemic infections with one or more unknown fungi immunologically closely related, possibly geotrichum.

CHEMOTHERAPY OF INFECTIOUS DISEASES

Aureomycin in the Treatment of Typhus Fever. FERIDUN TIMUR, Tekirdag, Turkey. Am. Pract. *2*:174-75, Feb. 1951.

The case history is cited of a 54 year old woman having murine typhus who responded dramatically to aureomycin.

Aureomycin treatment was initiated on the eleventh day of fever and was continued for three and a half days. The total amount of aureomycin administered was 8 Gm. during treatment. The first day of treatment consisted of a dose of 500 mg. every four hours (3 Gm. every 24 hours). This was followed by a dose of 500 mg. every six hours (2 Gm. every 24 hours) for an additional two and a half days. Within 12 hours after the onset of treatment, the temperature reached normal; the rash faded within 24 hours and disappeared within 48 hours. All the symptoms of the illness cleared up within 72 hours after the aureomycin was begun.

The treatment of typhus fever until the discovery of chloromycetin and aureomycin has been symptomatic. Aureomycin is justly considered as a specific for the entire group of typhus fevers. At present the daily oral dose for man seems to be 50 to 100 mg. per Kg., 3-6 Gm. daily for an adult, on a four to six hour schedule. 1 figure.—*Author's abstract.*

Chloramphenicol in Progressive Doses in the Treatment of Cases of Typhoid Fever of the Hypertoxic Type (*La chloromycétine à doses progressives dans le traitement des fièvres typhoïdes á forme hypertoxique*). M. E. FARINAUD (Médecin Colonel de T. C.) and L. PORTES (Médecin Capitaine des T. C.). Presse méd. *59*:3-4, Jan. 6, 1951.

A number of cases have been reported, especially in France, in which symptoms of collapse developed in patients with typhoid fever treated with chloramphenicol in the usual dosage; this has been attributed by some authors to too rapid lysis of the typhoid organisms and rapid liberation of their endotoxins. In their observations in Indo-China, the authors have observed the same phenomenon in cases of unusually severe typhoid fever. In 4 such cases treated with chloramphenicol in the dosage usually recommended, 50 mg. per Kg. as an initial dose and the same dose daily in divided doses, the blood cultures became negative and the temperature dropped, but vascular collapse or a bulbo-encephalitic syndrome developed and the patients died. In 1 case of severe typhoid fever, the initial dose was omitted and the daily dose diminished to 30 mg. per Kg. for the first day; then increased to twice that by the third day. In spite of a drop in temperature and negative blood cultures the patient developed delirium and symptoms of vascular collapse, but ultimately recovered. In 6 other cases of typhoid fever and 1 of paratyphoid A fever the dose in the first 24 hours was reduced to 15 mg. per Kg., and this was increased gradually, according to the clinical course of the disease. When the temperature fell to normal, the same dosage was continued for seven days. These cases all responded well to this method of treatment with complete recovery and no recurrence.

The authors are of the opinion that in cases of typhoid fever in which chloramphenicol therapy is begun promptly, the initial dose and large daily doses may be used on beginning treatment. But in cases in which treatment is delayed and symptoms of toxemia and debility are evident, the smaller dosage of chloramphenicol should be used at first and the dosage increased gradually but progressively until the temperature becomes normal. In such cases restoratives or desoxycorticosterone may be used as indicated in association with the chloramphenicol therapy.

Effectiveness of Aureomycin in Treatment of Tularemia. Report of Two Cases. ELMER S. ROBERTSON, Richmond, Va. Virginia M. Monthly. 78:71-73, Feb. 1951.

Recent reports have indicated that aureomycin is highly effective in the treatment of tularemia. The authors recently observed 2 patients with the ulceroglandular type, who showed excellent response. One was hospitalized; the other was treated successfully in the home.

Case No. 1:—A 60 year old white housekeeper was admitted to the hospital on January 12, 1950, complaining of high fever associated with a "sore" involving the left little finger. She was given aureomycin, one 250 mg. capsule every two hours for three days, then one capsule very four hours, 52 being the total number of capsules administered. Penicillin (duracillin, fortified, 1 cc. intramuscularly daily) was administered concurrently because of the secondary infection. Within 48 hours the temperature had returned to normal, and the lymphanitis was less marked. Within 72 hours the patient was clinically well.

Case No. 2:—The patient was a 52 year old white barber who, on December 26, 1949, had skinned a wild rabbit. Symptoms paralleled those of Case No. 1, with marked elevation of temperature, malaise, and the appearance of an ulcer on the finger. Aureomycin capsules (250 mg.) were given, two every six hours for four days, at which time the dosage was reduced to one capsule every six hours, the total number of capsules administered being 52. Within 36 hours the temperature, which had been 103, fell to normal and the symptoms subsided gradually.

In the 2 cases observed by the authors no untoward reactions to aureomycin were noted. A small quantity of food or milk was given just prior to the administration of the aureomycin to prevent the development of nausea or other gastro-intestinal disturbance. Although aluminum hydroxide has been administered with aureomycin in order to prevent nausea, it has been shown that the administration of alkali reduces the effectiveness of the drug and, for this reason, should not be used. Prior to the introduction of aureomycin, treatment of tularemia with streptomycin was found to be satisfactory. Other drugs, however, failed to prove effective. Sulfonamides showed questionable therapeutic effect, and penicillin was found to be of no value. Since there have been no harmful side effects reported with its use, aureomycin may prove to be the drug of choice in the management of tularemia. 6 references. 2 tables.—*Author's abstract.*

Q Fever in California. III. Aureomycin in the Therapy of Q Fever. WILLIAM H. CLARK, EDWIN H. LENNETTE, and GORDON MEIKLEJOHN, Berkeley, Calif. Arch. Int. Med. 87:204-17, Feb. 1951.

Forty-five patients with laboratory-confirmed Q fever were treated with aureomycin. In most instances, the method of choosing patients resulted in the treatment only of those moderately or severely ill. Data are also presented on 25 persons with Q fever who had been treated with penicillin alone.

Aureomycin was given orally, intramuscularly, intravenously, or by a combination of these routes. Dosages ranged from approximately 1 Gm. to 5 Gm. daily orally,

100-400 mg. daily by the intramuscular route, and either 200 or 300 mg. when the intravenous route was used. In the series treated with aureomycin, 49 per cent had become afebrile in three days following institution of therapy, 71 per cent became afebrile in five days or less. The median number of days of fever after treatment had begun was three days.

In the group treated with penicillin, 12 per cent had become afebrile within three days after treatment was begun, and 28 per cent became afebrile in five days or less. The median number of days of fever after therapy was begun was eight.

In addition to improvement as noted by a decline in fever, the majority of patients receiving aureomycin was subjectively improved within a few hours after therapy was begun; such subjective improvement was not observed among those receiving penicillin. In 4 patients treated with aureomycin, the clinical course of the illness appeared unaffected by the antibiotic. Since rickettsemia could be demonstrated in several patients for three days following initiation of treatment with aureomycin, it is suggested that the dosages employed may not have been entirely adequate. 7 references. 5 figures. 7 tables.—*Author's abstract.*

Chloromycetin in Infectious Mononucleosis. RUFUS F. PAYNE AND FRED CRENSHAW, Rome, Ga. J. M. A. Georgia *40*:75-76, Feb. 1951.

The author has reviewed two previously reported cases of infectious mononucleosis in which chloromycetin was effective. One was a patient who had manifestations of the disease for approximately a year and the other was a patient who had the disease for a relatively short time and was treated following a relapse.

The reported case was apparently acute in that the first blood count showed a marked leukopenia and occurred in a young white male. The temperature fell by crisis after approximately twelve hours and never again reached normal. The blood changes disappeared relatively early, except for the heterophile antibody, and at the end of four months there was no evidence of relapse.

It was the author's conclusion that the drug probably had some influence, as it would be most unusual for this type of case to remit by crisis and fail to show any evidence of the disease later. 2 references.—*Author's abstract.*

Treatment of Actinomycosis (Du traitement de l'actionomycose). F. FÖLDVÁRI, University of Eötvös Lórand, Budapest. Dermatologica *102*:77-88, No. 2, 1951.

Fifteen cases of actinomycosis treated with penicillin are reported. The actinomyces were found by direct microscopic examination in 9 cases, in 4 of which the cutaneous test was also positive; in 3 other cases the cutaneous test was positive, although the actinomyces were not found; in 2 cases both methods gave negative results, and the diagnosis was based on the typical clinical picture. Penicillin was used in the treatment of these cases, 200,000 units daily given in divided doses if an aqueous solution was used, or as a single injection in oil. Of the 15 cases treated, 10 were cured and 5 were improved. Of the 10 cases of the cervico-facial type 7 were cured and 3 improved; in this type of actinomycosis, the highest total dosage was 10 million units;

in 5 of the cases the total dosage was from 4.5 to 5.5 million units. In the cases with abdominal and pulmonary involvement, a higher total dosage was used, up to 20 million units. Cure was obtained in the 1 case of pulmonary involvement in this series. The author considers that penicillin therapy is the treatment of choice in actinomycosis. It can be employed when the patient is in poor general condition; it is effective in relieving the secondary inflammatory symptoms if these are caused by bacteria sensitive to penicillin. If the actinomycosis is due to a strain resistant to penicillin, the author prefers specific treatment with a vaccine and autohemotherapy. Sulfonamides, iodide, and x-ray therapy are employed only as a last resort.

Reiter's Syndrome: Apparent Recovery Following Treatment with Aureomycin. ARTHUR H. GRIEP AND CHARLES F. LEICH, Evansville, Ind. Univ. Michigan Med. Bull. *17*:18-21, Jan. 1951.

A 17 year old boy whose clinical picture satisfied the criteria for the diagnosis of Reiter's syndrome was treated with aureomycin, using a total of 24 Gm. over an eight day period. During this period of treatment he became asymptomatic with complete disappearance of the previously noted keratoconjunctivitis, urethritis, and arthritis. He received no further therapy and had remained asymptomatic during a one year follow up period. It is felt by the authors that further trials of aureomycin in patients with Reiter's syndrome is indicated.

Streptomycin Para-Aminosalicylate and Streptomycin Resistant Tubercle Bacilli. JOHN D. ADCOCK, Ann Arbor, Mich. Am. J. M. Sc. *221*:149-51, Feb. 1951.

Streptomycin para-aminosalicylate, in daily dosage equivalent to 1 Gm. of streptomycin (0.8 Gm. para-aminosalicylic acid), was given to a group of 12 patients having far-advanced, cavernous, pulmonary tuberculosis. Sensitivity determinations were done on tubercle bacilli recovered prior to therapy and at intervals during therapy. The rate of development of resistance to streptomycin was such that it could be concluded that the material was not effective in delaying the accumulation of resistant organisms. Two instances of exfoliative dermatitis were encountered. Decisive information regarding the effectiveness of various maneuvers in delaying streptomycin resistance may be obtained from small groups of properly selected patients. 8 references. 1 table.—*Author's abstract.*

Comparative Inadequacy of Present-Day Market Streptomycin in Tuberculosis. H. J. CORPER, M. L. COHEN, AND W. H. FREY, Denver, Colo. Rocky Mountain M. J. *48*:104-107, Feb. 1951.

The therapeutic efficiency of market streptomycin, as determined by the prolongation of life of normal, controlled guinea pigs infected intravenously with virulent human tubercle bacilli and maintained under standard experimental conditions, was found to be appreciably less in the 1949 preparations, as compared with those obtained in 1947.

The *in vitro* titer against acid-fast bacilli and human tubercle bacilli did not differ appreciably between the 1947 and 1949 market preparations making it appear that there is a lack of correlation between therapeutic efficiency of certain streptomycins and *in vitro* evaluations.

The foregoing findings would indicate the advisability of appropriate therapeutic efficiency tests for the determination of the value of streptomycin and other antibiotics in tuberculosis treatment. 10 references. 2 tables.—*Author's abstract.*

Terramycin: Clinical, Pharmacologic, and Bacteriologic Studies. R. J. SAYER, J. C. MICHEL, F. C. MOLL, AND W. M. M. KIRBY, Seattle, Wash. Am. J. Med. Sc. *221*:256-63, March 1951.

One hundred and eight cases of infections commonly encountered on the adult and pediatric medical wards of a general hospital were treated with terramycin. Adults received 1 Gm. of terramycin orally every six hours, and children were given doses of similar magnitude according to weight.

Blood levels of 2.5 to 10 micrograms per cc. were maintained for six to eight hours in adults after the oral administration of 1 Gm.; thereafter they declined, with levels of 0.1 to 0.5 micrograms per cc. remaining in the majority of the patients after 24 hours. Patients who received 1 Gm. every six hours maintained levels of 5 to 10 micrograms per cc. throughout the day.

Clinical improvement was noted in 24 (85 per cent) of 28 patients with urinary tract infections, and there was at least temporary urinary sterilization in 20 (71 per cent). Eighteen (86 per cent) of 21 children with pertussis responded to terramycin with clinical improvement. Favorable results were observed in 22 of 25 pneumonias in children and in all of 13 adults with bacterial pneumonias. Favorable responses were noted in patients with bacillary dysentery, tonsillitis, erysipelas, and bronchiectasis. A patient with typhoid fever had an excellent response to terramycin, both during the initial attack and during relapse. In one patient with subacute bacterial endocarditis and another with amebiasis definite clinical improvement was noted, although in both instances it was necessary to change to other chemotherapeutic agents. Two patients with mumps complicated by orchitis and one with infectious mononucleosis improved promptly when terramycin was administered. 3 references. 2 figures.—*Author's abstract.*

The Reactions of Bacteria to Chemotherapeutic Agents. L. P. GARROD, London, England. Brit. M. J. No. *4700*:205-10, Feb. 3, 1951.

Bacteria react in four ways to chemotherapeutic agents: suppression (which is the object of their therapeutic use), habituation, dependence, or stimulation.

Habituation, or acquired resistance, is exhibited by almost all species in relation to the sulfonamides and was seriously impairing the usefulness of these drugs before penicillin was introduced. Habituation to penicillin has not so far been an important obstacle to successful treatment, except in staphylococcal infections, although other species have sometimes been shown to undergo increase in resistance during pro-

longed treatment. There is so far no evidence of any general increase in bacterial resistance to penicillin as a result of its widespread use. The usefulness of streptomycin, on the other hand, is threatened with extinction owing to the facility with which all species can become highly resistant to it, the change being permanent. There is some evidence that a moderate degree of resistance can be acquired to aureomycin, chloramphenicol, and terramycin, which when it occurs as a response to one of them, involves all three.

Dependence on an antibiotic as a growth factor was first observed in organisms resistant to streptomycin: its development *in vivo* might conceivably cause therapeutic use to have the opposite of the desired effect. Dependence on chloramphenicol has also been observed and, in certain conditions, on penicillin.

The stimulation of bacteria by low concentrations of noxious agents is a well recognized phenomenon; a great variety of ordinary germicides actually enhance growth when only very small amounts are present. There is evidence of several kinds that the same is true of antibiotics. Penicillin in low concentrations has repeatedly been shown to accelerate bacterial growth. The author has verified that 0.004 unit and 4 units per ml. stimulate the growth of *Staphylococcus aureus* and *Pseudomonas pyocyanea*, respectively; several conditions affecting this stimulation have been identified. Such effects have also been observed experimentally *in vivo*, and "superinfections" with *Ps. pyocyanea* and other resistant organisms developing during penicillin treatment are probably explicable in the same way. If, as has been claimed, *Mycobacterium tuberculosis* is stimulated by penicillin, the incidental use of this drug in a case of tuberculosis might have harmful effects. 66 references. 4 figures. *—Author's abstract.*

The Synergistic Action and Potential Applications of Antibiotic Combinations. M. J. ROMANSKY, M. H. FUSILLO, E. CALDWELL, AND E. D. ROBIN, Washington, D. C. Med. Clin. North America *34*:535-44, March 1951.

Although indications for the newer antibiotics (aureomycin, chloromycetin, and terramycin) as well as penicillin and streptomycin are reasonably specific, certain bacteria by in vitro studies have developed resistance to penicillin, streptomycin, aureomycin, chloromycetin, and terramycin.

Data from 1943 to 1949 shows an increasing resistance to penicillin of the hemolytic staphylococcus aureus, hemolytic staphlyococcus albus and the nonhemolytic streptococcus. In the same period all of the common types of gram-negative organisms have shown by in vitro studies a marked increase in resistance to streptomycin. Of the gram-positive organisms the hemolytic staphlyococcus aureus and the alpha streptococcus viridans also show this trend.

Generally speaking, except for tuberculosis where streptomycin and para-aminosalicylic acid are specifically indicated, and in occasional instances where the combination of streptomycin with the other antibiotics will be effective, there is little indication for streptomycin to be used initially.

Current in vitro studies also show increasing resistance of certain bacteria to aureomycin and terramycin. A lesser degree of resistance has occurred to chloro-

mycetin. The alpha streptococcus fecalis (enterococci) have always shown a relative resistance to penicillin. This group of organisms are sensitive to aureomycin, chloromycetin, and terramycin, but their effect is bacteriostatic. Laboratory and clinical studies indicate that for infections due to this organism, combinations of penicillin with aureomycin, terramycin, streptomycin, or chloromycetin, in that order, are indicated.

For the initial treatment in infections due to *Esch. coli* and *aerogenes* the newer antibiotics can be used (aureomycin, chloromycetin and terramycin). For proteus infections chloromycetin is the antibiotic of choice, by oral or by the intravenous route. The more soluble sulfonamides alone or with chloromycetin may be effective. Aureomycin or terramycin may be helpful with chloromycetin, but generally this organism does not respond to either when given alone. *Pseudomonas aeruginosa* infections are most effectively treated by combinations of the new antibiotics, for example, chloromycetin with aureomycin, terramycin, or streptomycin.

The combination which appears to be least effective is aureomycin and terramycin, since studies of the authors indicate that resistance of various organisms to aureomycin and terramycin develops simultaneously.

Subacute bacterial endocarditis due to alpha hemolytic streptococcus (viridans) is still best treated with penicillin alone in adequate doses unless the organism is resistant. If so, the newer antibiotics are effective in infections due to this bacteria. The cumulative effect of aqueous procaine penicillin makes it particularly helpful in the treatment of subacute bacterial endocarditis and other severe infections which require high concentrations of penicillin in the blood.

Bacteremias and endocarditis due to hemolytic staphylococcus aureus and hemolytic staphylococcus albus should be treated with penicillin plus chloromycetin or aureomycin or terramycin. 14 references. 8 tables.—*Author's abstract.*

Combined Administration of Desoxycorticosterone Acetate and Ascorbic Acid. II. Experimental Observations. C. A. SCHAFFENBURG, J. B. R. MCKENDRY, AND E. PERRY MC CULLAGH, Cleveland, Ohio. Arch. Int. Med. *87*:199-203, Feb. 1951.

The effects of combined administration of desoxycorticosterone acetate (DCA) and ascorbic acid to mice and rats were studied by means of the "cold test," egg-white reaction and formaldehyde-induced arthritis. It was found that the combination of DCA and ascorbic acid exerted no cortisone-like activity and ascorbic acid failed to modify the organic (renal, cardiac) lesions as well as the functional derangements (increase in blood pressure and diuresis) resulting from DCA overdosage. 17 references.—*Author's abstract.*

Penicillin Levels in Spinal Fluid after Intramuscular Injection of Procaine Penicillin. R. D. WRIGHT, Washington, D. C. J. Ven. Dis. Inform. *32*:39-42, Feb. 1951.

Penicillin levels were determined on 198 specimens from 114 patients at intervals ranging from 2 to 290 hours following the first injection. Injections of 600,000 units

of commercial procaine penicillin suspended in sesame oil containing 2 per cent aluminum monostearate were given every 24 hours for six doses. Detectable levels of penicillin were obtained in 82 per cent of the specimens at 31 hours and 91 per cent at 122 hours. In a second group of 22 patients receiving one intramuscular injection of 300,000 units of procaine penicillin in oil with 2 per cent aluminum monostearate, 4 of the specimens showed a measurable level, and 8 showed a trace. 7 references. 1 figure. 2 tables.—*Author's abstract.*

Neomycin: Results of Clinical Use in Ten Cases. G. G. DUNCAN, C. F. CLANCY, J. R. WOLGAMOT, AND B. BEIDLEMAN, Philadelphia, Pa. J.A.M.A. *145*:75-80, Jan. 13, 1951.

It has been shown that a wide variety of pathogenic organisms insensitive to antibiotics in current use were sensitive to neomycin in vitro. Ten cases in which neomycin therapy was employed are reported. Each patient had a bacterial infection due to one or more pathogenic organisms which were completely or moderately resistant to penicillin, aureomycin, chloramphenicol, and streptomycin, while all but one—a *Pseudomonas*—were known to be sensitive to neomycin.

Four cases of pyelonephritis, 4 cases of cystitis, and 2 cases of bacteremia were treated. The pathogenic organisms included *A. aerogenes, Ps. aeruginosa, Esch. coli, paracolon bacillus*, coliform bacilli, nonhemolytic *Streptococci, Proteus*, and hemolytic *Staphylococcus aureus*. Results were favorable in 8 of the 10 cases.

Neomycin was given intramuscularly, in doses varying from 4,498 units (to an infant) to 100,000 units at six hour intervals. The duration of therapy varied from three to nine days. In the infections due to a sensitive organism, 100,000 units at six hour intervals for four doses and thereafter 50,000 to 100,000 units at 12 hour intervals for five to seven days ordinarily appeared adequate, but dosage required regulation in accord with the desired blood and urine concentrations of neomycin, which in turn are related to the sensitivity of the organism. The concentrations of neomycin in the serum and urine were built up gradually, usually reaching a maximum after 48 to 72 hours of therapy. After adequate therapeutic levels had been achieved, the serum and urine levels remained relatively stable on either a 6 or 12 hour schedule. The maximum serum levels varied from 4 to 10 units per milliliter, but in patients with poor renal function rapidly built up to and in excess of 16 units. Maximum urine levels varied from 26 to 410 units per milliliter. Measurable quantities of the drug persisted in the serum for 24 to 36 hours after cessation of therapy, while urinary excretion continued in declining amounts for 48 to 72 hours after treatment had ceased.

Neomycin was dramatically effective in eradicating organisms sensitive to it from the blood and urinary tract. It is considered significant that in no case in which the sensitive organism was eradicated did it return after cessation of therapy. The original observations of Waksman and Lechevalier on the bactericidal properties of the drug were confirmed.

Apparent evidences of toxicity were confined to one patient and consisted of impaired hearing and an increased blood urea nitrogen level. Improved hearing followed cessation of therapy, but elevation of the blood urea nitrogen values persisted.

Although proof of the direct relationship between neomycin therapy and these changes is lacking, it is believed that treatment with the drug should be discontinued in any patient manifesting impaired hearing or urea nitrogen retention while receiving neomycin.

It is concluded that neomycin is an extremely effective agent in the treatment of clinical infections, particularly those of the urinary tract. 4 references. 1 table. 1 chart. —*Author's abstract.*

Folic Acid and Histamine. V. TRAINA, Cleveland, Ohio. Ann. Allergy *9*:229, March-April 1951.

Folic Acid given intraperitoneally in the dose of 100 mg. per Kg. of body weight appears to protect guinea pigs from an intracardiac injection of 0.4 mg. per Kg. of histamine. Such protection is lost when higher doses of histamine are used, even if the previous injection of folic acid is increased to 150 mg. per Kg. of body weight. 8 references.—*Author's abstract.*

DISEASES CAUSED BY ANIMAL PARASITES

Toxoplasmosis Due to Laboratory Infection in Two Adults. J. STORM, Stockholm, Sweden. Acta med. Scandinav. *139*:244-52, f. 1, 1951.

After a brief survey of the occurrence and symptomatology of congenital toxoplasmosis, a review is presented of the few existing reports of acquired toxoplasmosis. Generally the infection seems to have an inapparent course, but in 2 children and 1 adult it has caused acute meningoencephalitis and in 1 adult chronic meningoencephalitis. In 2 other adult cases the course was that of an acute infectious disease, with maculopapular exanthema, interstitial pneumonia, myocarditis, and encephalitis. Only in 1 case did the patient survive.

An account is then given of laboratory infection with toxoplasma material in two women, both 22 years old. One was probably infected per os; the other was infected by pricking a finger. The diagnosis in both cases was established by strongly positive dye tests.

The patient infected per os became severely ill. At the outset her general condition was affected; there were chills, fairly high remittent temperature, painful inflammation of the cervical glands, conjunctivitis, headaches, and pain over the eyes. The fever persisted, abating gradually for two weeks. On the third day maculopapular exanthema appeared on the trunk, disappearing in two weeks and followed by scarlatiniform desquamation. Enlargement of the lymph nodes became general and persisted for two months. In the beginning the blood picture showed slight anemia and leukopenia. The sedimentation rate was at first slightly increased, then rose to 53 mm. and became normal after one month.

Meningitis with mild pleocytosis was manifested after one week's illness. The electroencephalogram showed no pathologic features, but during convalescence the patient

suffered from headaches, pronounced mental exhaustion with greatly impaired ability to concentrate, and frequent absences reminiscent of petit-mal, which showed that encephalitic changes were also present. No intracranial calcifications developed and no inflammatory foci were found in the eye grounds. After three weeks, symptoms of myocarditis occurred, with anginal pains and moderate symptoms of insufficiency, as well as electrocardiographic changes. The symptoms persisted for six months.

In the other case, in which the patient was infected through inoculation in a finger, only a local infection ensued after three days, with mild lymphangitis and lymphadenitis in the axilla and a rise in temperature for 24 hours. All other tests carried out showed negative results.

Congenital Toxoplasmosis. Case Report with Autopsy Findings. E. SCHRICK, Oakland, Calif. Perm. Found. Med. Bull. *9*:44-48, Jan. 1951.

As there have been only 21 cases of infantile toxoplasmosis with autopsy findings reported in the literature, it was considered worthwhile to add this typical case.

C. J. H. was a two month premature female infant born February 21, 1950, weighing 3 lb. 13 oz. at birth. The anterior fontanel measured 4 x 5 fingerbreadths and had a doughy consistency. The infant had routine premature care in 0_2 and incubator, and 10,000 units procaine penicillin every three hours prophylactically for six days. She gained weight slowly.

No marked abnormality was noted until the fifth week of life when the left eyelids became swollen, and the anterior fontanel was larger, with marked diastasis of the coronal sutures. A lumbar puncture showed xanthocromic spinal fluid to be present under increased pressure, containing 69 white blood cells per cubic millimeter, 675 milligrams of protein per 100 cc. and 52 milligrams of sugar. Spinal fluid culture produced no growth of organisms. The differential diagnoses considered were:

(1) hydrocephalus (2) meningitis, etiology unknown; (3) microphthalmus, left; (4) possible subdural hematoma; (5) possible tumor of the third ventricle.

Bilateral subdural taps were done to rule out subdural hematoma. Air encephalograms showed large, dilated lateral ventricles with no communication with the third ventricle. Skull x-rays did not show any calcified areas in the brain. Left eye examination revealed: (1) blepharophimosis, (2) an abnormal pupil, (3) white mass in vitreous which might be due to proliferating chlorioretinitis, secondary to toxoplasmosis. Right eye examination was normal.

The complement fixation test for toxoplasmosis was negative in this case.

Treatment for toxoplasmosis is very unsatisfactory. Penicillin and sulfadiazine were tried, and the infant was transfused as often as necessary.

The course of the disease was afebrile and gradually down-hill until death occurred on the sixty-ninth day.

The autopsy findings were central nervous system necrosis, dilated lateral ventricles due to obstruction of the sylviduct, microscopic calcifications, pseudocysts in brain, leptomeningitis, chorioretinitis, and involvement of the heart muscles. 4 references. 8 figures.—*Author's abstract.*

RESPIRATORY DISORDERS AND DISEASES

Combined Intracavernous Conteben (TB 1) Therapy (Die combinierte intracavernöse Conteben (TB 1) Therapie). HAROLD MALLUCHE, Landesheilstatte Falkenstein/Ts., Germany. Acta med. Scandinav. *139*:105-21, Jan. 31, 1951.

The treatment of tuberculous patients with large cavities, by the instillation of thiosemicarbazon (TB 1 or Contaben) into the cavity combined with drainage of the cavity by the Monaldi method and the administration of TB 1 by mouth in a daily dosage of 0.05-0.1 Gm. is reported. When the drainage tube is in place, 0.1 Gm. TB 1 in 20 per cent glycerine suspension is injected into the cavity; this is done in the evening, and the Monaldi suction drainage is carried out during the day. As it has been found that there is sometimes a secondary infection of the drainage canal with Monaldi drainage, ten to twenty thousand units of penicillin are injected daily or every other day into the cavity. If the introduction of the drainage tube causes a febrile reaction, streptomycin is given for six to eight days, as a rule, never for more than 14 days, ¼ Gm. instilled into the cavity, and ¼ to ½ Gm. given intramuscularly. The treatment of the cavity with TB 1 is continued until no more tubercle bacilli are demonstrated in the material drained from the cavity. In some cases PAS has been used with the TB 1 treatment, but streptomycin is used only as noted above. No evidence of the development of TB 1-resistant strains of tubercle bacilli has been found. This method of treatment has been employed in 100 cases with closure of the cavity resulting in each case. Toward the end of the treatment the pressure used for suction drainage is always reduced. While the cavity can be closed by this method of treatment, supplementary collapse therapy is necessary to ensure permanent closure of the larger cavities; and in some cases thoracoplasty will be indicated. 7 figures.

Streptomycin Failures in Tuberculosis. RUFUS F. PAYNE, Rome, Ga. J.M.A. Georgia *40*:20-22, Jan. 1951.

The author presents data on the type tuberculosis which is least likely to respond to treatment with streptomycin. He stresses early diagnosis of tuberculous meningitis as being essential if treatment is to be successful and quotes figures to show that cases treated early have a much better prognosis than those treated later in the disease.

He also presents data to show that, in lesions such as bone, kidney and other extra pulmonary tissues, drainage is essential once the lesion has progressed to the point of caseation and suppuration. Streptomycin alone is usually insufficient to bring about healing once the tissues have broken down.

The author states further that failures in treatment of pulmonary tuberculosis are much more likely to occur if the lesions are fibro-cavitary in character, if chronic, and if the lesion is unsuitable for collapse therapy of any type. He stresses the fact that, once lesions have resolved under the influence of streptomycin, it is most essential that bed rest and collapse measures be carried on for a sufficient length of time for the tissues to heal, as it is quite apparent that streptomycin within itself does not hasten histologic changes which occur in the healing process.—*Author's abstract.*

Basedowian Condition with a Familial Character: Its Relation to Tuberculosis. P. DELORE AND G. NOEL, Lyons, France. Présse med. *59*:245-46, Feb. 1951.

As the role of heredity and tuberculosis in Grave-Basedow's disease has been discussed, the writers report 10 cases, which, with the addition of many others they found in the literature, allow them to make the following statements:

1. The coexistence of dysthyroidism of basedowian type in females of the same family is not infrequent.

2. When an inquiry is systematically and deeply conducted about the existence of tuberculosis in the family history of a basedowian, the disease is found to have been present in about two thirds of Basedowism cases.

3. Tuberculosis, a disease essentially familial, is susceptible of accounting for the familial character of certain basedow's syndromes.

4. Similar observations were reported by P. Delore as regards certain cases of acute articular rheumatism (Bouillaud's disease), so that an association of this disease with Basedow's syndrome may be suggested as both being possibly influenced by a tuberculous inheritance more or less distant in the past.

Antibiotics in the Treatment of Purulent Tuberculous Pleurisy (Les antibiotiques dans le traitement des pleurésies purulentes tuberculeuses). PEAN LARDANCHET AND CHARLES STUDER, Neufmoutiers-en-Brie, France. Presse méd. *59*:96-98, Jan. 24, 1951.

Two cases of purulent tuberculous pleurisy are reported with a pleuropulmonary fistula, which were treated by the local and parenteral administration of streptomycin with discontinuous aspiration. One of these patients was treated before PAS became available; in the other PAS was used in association with the streptomycin. In both the pleuropulmonary fistula closed, and pleurisy cleared up. In addition to these 2 cases, the authors have treated 4 other cases of tuberculous pleurisy with pleuropulmonary fistula, in which the development of the lesion was more gradual and the general health of the patient was not so seriously affected as in the 2 cases reported. In 3 of these cases healing of the fistula and clearing of the pleurisy were obtained by antibiotic therapy and discontinuous aspiration, but in 1 case the pleurisy recurred and thoracoplasty was necessary to obtain a cure. 4 figures.

Medical Care Problems in a Group of Patients with Chest Pathology. LEE POWERS, Seattle, Wash. Northwest Med: *50*:26-30, Jan. 1951.

The article reports the results of an attempt by direct interview to obtain the reason why some patients with subjective and objective findings of a disease either do not consult a physician or do not reasonably attempt to follow the physician's advice when they do seek help.

The patients interviewed were those discovered in a mass roentgen survey in Pierce County, Washington (Tacoma), in which 72,703 seventy-millimeter (46 per cent of population over 15 years of age) films were taken and 1,462 were recalled for 14 x 17 inch films; of those, 645 were interviewed by the usual interview methods. Subjective

symptoms reasonably chargeable to pathology were present in 399 or 53 per cent.

Tuberculosis or suspected tuberculosis was found in 224 of the 339 with symptoms, and the balance (115) presented other abnormal findings. Ninety-two patients who had subjective symptoms had never consulted a physician. The reasons in order of frequency were: (1) did not understand importance of the symptoms, 70 per cent, (2) symptoms mild or of short duration, 16 per cent, (3) economic reasons, 4 per cent, (4) miscellaneous, 10 per cent.

There were 77 patients who had symptoms and consulted a physician but did not reasonably attempt to carry out his recommendations. Reasons given in order of frequency: (1) did not understand importance of symptoms, 31 per cent, (2) economic, 22 per cent, (3) lack of confidence in medical science, 19 per cent, (4) fear, 12 per cent, (5) miscellaneous or not stated, 16 per cent.

The combined reasons given by patients for either not seeking care or not following their physicians' recommendations in order of frequency are: (1) misunderstanding of importance of the symptoms, 52 per cent, (2) economic, 12 per cent, (3) symptoms mild or short duration, 10 per cent, (4) miscellaneous, 8 per cent, (5) fear, 7 per cent, (6) not stated, 1 per cent.

The author pointed out many factors present to bias the study and states that, strictly speaking, the findings of the survey are true only within the limitations of the survey. He suggests the same technic be used in larger numbers of cases to determine directly how frequently ill persons do not receive proper medical care because of financial reasons. 13 tables.—*Author's abstract.*

The Lung Function During Rest and Exercise in Lung Diseases. A Bronchospirometric Study. S. BJORKMAN AND E. CARLENS, Stockholm, Sweden. 1st Internat. Cong. Int. Med. p. 57-62, 1950.

A new type of flexible double lumen catheter, which can be placed in position without the aid of fluoroscopy, has been constructed for the purpose of examining the function of each lung separately. This instrument makes it possible to carry out bronchospirometric examinations not only during rest but also during exercise. A cycle ergometer, on which the subject is able to exercise in the horizontal position, has been built for the exercise tests.

During oxygen-enriched air breathing, moderate exercise does not alter the correlation between the oxygen consumption in the two lungs, measured under basal conditions. Twenty-two cases of different lung diseases have been examined.

The oxygen consumption of each lung during rest has been studied in 16 cases of different lung diseases, both during oxygen-enriched air breathing and during breathing of ordinary air with a constant 0_2 content. It seems evident that the function of the inferior lung deteriorates during ordinary air breathing as compared with the results during oxygen-enriched air breathing.

In order still further to refine the functional tests, trials are in progress in which the patient is examined during exercise, breathing ordinary air with a constant 0_2 content and also breathing ordinary air with one lung and oxygen-enriched air with the other.

Arterio-Venous Fistula of the Lung. Report of 4 Cases, Including an Acyanotic Case. H. A. SALVESEN AND F. MARSTRANDER, Oslo, Norway. Acta med. Scandinav. *139*:167-75, f. 3, 1951.

After a short review of the literature 4 cases of arteriovenous fistula of the lung are described, in 1 man of 37 and 3 women of 25, 21, and 42. The diagnosis was established by planigraphy in 3 patients and confirmed by successful operation in the man; an incipient lymphogranulomatosis prevented operation in one of the women and the third patient declined surgical treatment. The condition was also diagnosed retrospectively in a fourth patient, a woman of 21, who in 1934 had obtained the unsatisfactory diagnosis of morbus caeruleus, as no heart disease could be found. We now found that the case report contained all the characteristic signs of arteriovenous fistula of the lung including a characteristic x-ray picture of a tumor of the right lung. The blood flow through the shunt was calculated to amount to more than 30 per cent of the total blood flow.

In addition to the cyanosis, polycythemia, clubbed fingers, normal heart and spleen, the first patient had hemangiomas of the lips, skin, nasal muscosa and probably of the central nervous system as he died from subarachnoidal hemorrhage, two and one-half years after the operation. In one of the cases (a woman of 42) in which the cyanosis, polycythemia, and clubbing of the fingers were absent, the heart was found to be enlarged and the diagnosis came as a surprise on routine x-ray examination. The reason for the heart enlargement, which is unusual in this condition, is discussed.

CARDIOVASCULAR DISORDERS AND DISEASES

Subacute Bacterial Endocarditis Due to H. para-influenzae and Str. viridans. J. G. GOUDIE AND C. P. LOWTHER, Glasgow, Scotland. Brit. M. J. No. *4700*:217-18, Feb. 3, 1951.

In the case of a young woman admitted to the hospital with pyrexia of six weeks' duration, the diagnosis of subacute bacterial endocarditis was made on the basis of altering cardiac murmurs, slight embolic phenomena and positive blood culture, yielding *Str. extracaccus viridans* and gramnegative filaments. Treatment with penicillin for 51 days (224 million units), followed after a week by four days' treatment with aureomycin (4 gm.) and then 13 days' treatment with streptomycin (26 gm.) led to an excellent recovery.

After penicillin therapy, blood cultures yielded only the bacillus, identified as *H. para-influenzae;* this disappeared from the blood after the administration of streptomycin; *in vitro* it was resistant to 10 units of penicillin, but suppressed by 1.6 μ g. of streptomycin per ml. of medium. A method of preparing a stable suspension of *H. para-influenzae* for agglutination reactions is described, and the unusually long survival (11 weeks) of the organism in blood cultures is noted. The reasons are discussed for believing that *H. para-influenzae* played a part in the causation of the disease. 13 references.—*Author's abstract.*

Antistreptolysin Titer as an Aid in the Diagnosis of Rheumatic Fever. B. B. BREESE, Rochester, N. Y. New York State J. Med. *51*:389-91, Feb. 1951.

Antistreptolysin O is an antibody produced in the sera of patients in response to a beta hemolytic streptococcal infection. Most investigators have found the titer of this antibody elevated in the majority of patients with rheumatic fever. In the Rochester (N. Y.) hospitals and in the Rheumatic Fever Clinic we have found the test of value as an aid in the diagnosis of rheumatic fever. Our material was divided into four groups: (1) *normal*—160 children sent to the rheumatic fever clinic who had no evidence of rheumatic fever; (2) *Possible, probable, or definite rheumatic fever, inactive*—45 patients with histories or physical findings suggestive of past rheumatic fever but at present inactive; (3) *Known streptococcal infections*—39 children not treated with penicillin with proved beta hemolytic streptococci infections, most of whom had mild infections; (4) *Definite active rheumatic fever*—56 patients with unquestioned rheumatic fever, the majority with fever, polyarthritis, and evidence of carditis.

Titers of 250 units or above were considered abnormal. The results were as follows:

Classification	*Per cent* 250 *or above*
"Normal"	24
Possible, probable, or definite past rheumatic fever	42
Streptococcal infections	60
Definite active rheumatic fever	95

Common Errors in the Management of Acute Myocardial Infarction. A Critical Analysis of 58 Fatal Cases. D. S. RUBSAMEN, Chicago, Ill. California med. *74*:115-17, Feb. 1951.

This article analyzes the management of 58 fatal cases of acute myocardial infarction with special attention given to the well-accepted principles of rest, relief of pain, and control of arrhythmias. The patients were selected consecutively from admissions to a private hospital.

Three prominent errors were observed. First, pain was relieved inadequately in 23 cases, 14 of them experiencing severe pain (described variously as "unbearable," "excruciating," and "very severe") for more than two hours after entry. Although the initial administration of a narcotic to these patients was prompt, three or four hours often elapsed between injections. Intravenous sedation was rare, and 5 patients were in shock, thus absorbing little of the subcutaneously injected medication. Second, 7 patients who complained little of pain were sedated inadequately. Restlessness and excess activity resulted; 2 of them suffered left ventricular rupture, and 2 others died abruptly but were not autopsied. Third, in 3 cases sudden, painless death was preceded by irregularities of cardiac rhythm which were noted but not treated. These patients were improving from moderately severe infarcts. In 6 cases atypical pain or obscure electrocardiographic patterns prevented diagnosis until autopsy. One-third of the patients received dicumarol, and only one thrombo-embolic phenomenon (in the untreated group) occurred. 1 reference.—*Author's abstract.*

Since in our experience low titers of antistreptolysin O in definite active rheumatic fever are uncommon, the presence of a low titer is of considerable value in ruling out a diagnosis of rheumatic fever. A high titer, however, does not indicate rheumatic infection, activity or prognosis. 16 references. 2 tables.—*Author's abstract.*

Instillation of Streptomycin into the Pericardial Sac in Tuberculous Pericarditis. R. P. K. COE, London, England. Brit. M. J. No. *469*:18-19, Jan. 6, 1951.

Several cases of tuberculous pericarditis treated with streptomycin by the intramuscular route have been reported in the literature. Reference is made in a report of the Medical Research Council (1950) to one case of tuberculous pericardial effusion in which streptomycin was injected into the pericardial sac, but no details or dosage were given. Tapie et al (1950) also report the case of a man of 44 with chronic pulmonary tuberculosis who developed a pericardial effusion. They gave five injections of streptomycin, totalling 1.15 Gm., into the pericardial sac without obvious improvement.

A Post Office electrician aged 20, whose brother was suffering from a pleural effusion, was found to have enlarged hilar glands on mass radiography. Three months later he developed substernal pain, malaise, fever, and vomiting, and two weeks later he was admitted to hospital.

On examination he was found to have a large pericardial effusion with moderate engorgement of the neck veins and pulsus paradoxus. Pericardial paracentesis yielded dark straw-colored fluid which grew *Mycobacterium tuberculosis* on guinea pig inoculation, but direct smears and Lowenstein culture were negative.

He developed cardiac tamponade, which was rapidly relieved by aspiration of 32 ounces (907 ml.) of fluid. Intramuscular streptomycin ½ Gm. b.d. failed to control the fever, and the effusion re-accumulated rapidly with recurring tamponade, which necessitated six further aspirations, the amounts varying from 14 to 32 ounces (397 to 907 ml.) over the next seven weeks. Six injections of 1 Gm. of streptomycin dissolved in 2 ml. of water were therefore given at weekly intervals into the pericardial sac in addition to the intramuscular injections. The temperature slowly subsided shortly after this, and the pericardial effusion reformed very slowly, only 6 ounces (170 ml.) being aspirated on two occasions thereafter.

The patient subsequently developed a left pleural effusion, superior mediastinal obstruction from a large mass of glands in the upper mediastinum, hepatomegaly, ascites, and edema of the legs, without any notable recurrence of fever or toxemia, and all these manifestations slowly subsided on further bed rest. He was back at full work and in very good health 18 months after the onset of the illness.

It is suggested that streptomycin injected into the pericardial sac in conjunction with streptomycin by the intramuscular route constitutes a safe and rational form of treatment of tuberculoua pericardial effusion, especially when there is rapid reaccumulation of fluid.

I wish to thank Dr. J. B. Harman for permission to publish this case. 2 references. 1 table.—*Author's abstract.*

The Prognosis in Arterial Hypertension: Report on 117 Patients under 53 Years of Age Followed 8 to 10 Years. A. H. GRIEP, Evansville, Ind., G. R. BARRY, Monroe, Wisc., W. C. HALL, San Diego, Calif., and S. W. HOOBLER, Ann Arbor, Mich. Am. J. Med. Sc. *221*:239-49, March, 1951.

Of 117 carefully studied hypertensive patients under the age of 53 with blood pressures initially exceeding 160/110 who were followed up nine years later, 46 per cent had died of the complications of hypertensive disease. Cerebrovascular accidents accounted for approximately one half of the deaths, and cardiac and renal complications accounted for the remainder.

The most important factor in determining prognosis was the initial presence of vascular disease as manifested by cardiac enlargement, electrocardiographic alterations, albuminuria, or hypertensive encephalopathy. Approximately 80 per cent of patients with such complications died, whereas only 20 per cent of those without evidence of vascular damage failed to survive the nine year interval. The effect of such complications on mortality rate was independent of the height of the blood pressure, sex distribution, or other known variables.

In addition to the above, certain findings of lesser individual prognostic value were: (1) the height of the blood pressure; (2) sex of the patient (mortality rate in males was higher by a ratio of 3:2); (3) degree of hypertensive retinopathy. The age of the patient and duration of hypertension had little, if any, effect on the outcome.

It was generally impossible to predict the type of death from the findings at the initial examination.

The survivors, when re-examined, showed evidence of slow progression of their hypertensive disease. However, 80 per cent were without serious or disabling symptoms. The benign course of the disease in many patients without vascular complications is emphasized.

The blood pressure showed little tendency to change either in the survivors or in those who died of hypertensive disease. Many patients withstood severe hypertension for many years; only 2 survivors had a fall in blood pressure to normal levels.

The unreliability of the height or change in the blood pressure level as a prognostic sign in hypertension is emphasized, and the importance of determining the degree and progression of vascular damage in heart, brain, kidneys, and retina is stressed. Such data must be known before mortality rates in any series of hypertensive patients can be evaluated, and this information is of vital importance in formulating a plan of treatment for a patient with "essential" hypertension. 15 references. 2 figures. 2 tables.—*Author's abstract.*

Veratrum Viride in the Treatment of Essential Hypertension. A Report of 40 Cases. FREDRIC B. FAUST, Littlefield, Texas. Journal Lancet *71*:65-8, Feb. 1951.

Forty ambulatory patients with sustained hypertension, ranging in age from 25 to 78 years, were observed. A diagnosis of essential hypertension, with a detailed history and complete physical examination in each case, was confirmed by two investigators. Urinalysis, urine concentrations, and intravenous pyelography were used to evaluate

renal function. Cardiac studies included electrocardiograms and roentgenologic examinations. For purposes of analysis, the results were divided into (1) patients exhibiting side reactions, (2) patients under 50 years of age, (3) patients with high systolic blood pressures, (4) patients with high diastolic blood pressure, and (5) patients with cardiac decompensation.

Due to the prolonged action of the drug, vertavis should be administered during morning and evening hours, the first dose in the morning and the first dose in the evening separated by 12 hour intervals; not more than one tablet is given in any one hour. As described by other investigators, the therapeutic dose of vertavis is unrelated to the age of the patient, the severity of the disease, the elevation of blood pressure, or the duration of the hypertension. In this series of patients, the dose varied from 20 to 60 Craw units daily. In all cases dosage was given without interruption.

The results of treatment were as follows: basal blood pressure level—174/100, cold pressor response (immediate)—180/100, cold pressor response (in 20 min.)—180/100. The results following therapy with vertavis for one month were: basal blood pressure level—144/90, cold pressor response (immediate)—153/90, cold pressor response (20 min.)—130/78. Changes in blood pressure, together with length of treatment and dosage show that, in general, blood pressure response was prompt in the youthful group and was notably slower in the group of patients with high diastolic pressure. Reversal of left ventricular strain pattern was observed in the electrocardiogram following vertavis therapy. The temperature is to seek a cardinal sign for such disease. In hypertension, however, more than blood pressure is involved; the problem is not entirely a matter of hemodynamics. For that reason, we are inclined to describe hypertension as *hyperpiesis*, a term expressing increased tension including increased blood pressure, applied by Albutt at the turn of the century. We reintroduce this term, not to be pedantic, but to stress an important phase in our medical thinking.

It may be concluded that: 1. Forty cases of essential hypertension were treated up to a period of nine months with veratrum viride biologically standardized as the whole-powdered drug.

2. In the majority of cases significant lowering of both systolic and diastolic blood pressure was observed.

3. Side reactions consisting of nausea and vomiting were noted in 5 cases. Fine adjustment and control of dosage minimized these reactions in 4 of the 5 cases; in 1 patient the drug had to be discontinued.

4. In general, agreement was found with Freis that "veratrum viride has produced the most marked reduction of blood pressure in the greatest number of cases." 10 references. 4 figures. 5 tables.—*Author's abstract.*

Role of Somatotrophic Hormone in the Production of Malignant Nephrosclerosis, Periarteritis Nodosa, and Hypertensive Disease. HANS SELVE, Montreal, Canada. Brit. M. J. No. *4701*:264-70, Feb. 10, 1951.

Experiments on female piebald rats revealed that electrophoretically pure somatotrophic hormone (S. T. H.) produces nephrosclerosis with variable degrees of

nephritis, marked polyuria, myocarditis, pancreatic periarteritis nodosa, and hypertension. The experimental animals were sensitized to mineralo-corticoid actions by unilateral nephrectomy and an excess NaCl intake, but this sensitization in itself did not produce such changes.

The type of the toxic manifestations, as well as the sensitization of the animals to these S.T.H. effects by the unilateral nephrectomy and NaCl, parallel our previous findings in animals receiving excesses of desoxycorticosterone acetate (D.C.A.) or lyophilized anterior pituitary (L.A.P.) material.

It is assumed that S.T.H. is the active principle responsible for the toxic actions of L.A.P. upon the kidney and the cardiovascular system. The lesions caused by S.T.H. are considered to be, in all likelihood, secondary to a sensitization of the tissues to D.C.A. like mineralo-corticoids. In addition, S.T.H. may also increase the production of mineralo-corticoids by the adrenals.

The cardiovascular and renal damage normally caused by S.T.H. overdosage is prevented if cortisone is simultaneously administered in doses adequate to produce adrenocortical atrophy.

S.T.H. increases the sensitivity of the rat to the production of experimental arthritis. Simultaneous treatment with cortisone exerts a contrary effect. However, larger doses of cortisone are required to inhibit an experimental arthritis in the S.T.H.-treated than in the otherwise untreated animal. Apparently the anti-arthritic effect of cortisone is inversely proportional to the amount of S.T.H. present in the organism.

In the production of the so-called "diseases of adaptation" S.T.H. appears to play a part equally as important as that of ACTH. The former is responsible for the activity of mineralo-corticoids, which stimulate defensive granuloma formation, while the latter regulates the secretion of gluco-corticoids, which inhibit such defense reactions. 20 references. 12 figures. 4 tables. 1 chart.—*Author's abstract.*

Thiocyanate Therapy of Hypertension. Further Experiences. K. AAS AND R. THINGSTAD, Oslo, Norway. Acta Med. Scandinav. *139*:229-41, f. 1, 1951.

The effects of potassium thiocyanate on blood pressure and subjective symptoms were investigated in a hospital material comprising 40 patients with essential hypertension. It was sought to keep the concentration of thiocyanate in plasma at from 7 to 12 mg. per cent. Only in some few cases was the concentration higher for a short period. Toxic symptoms in the form of exanthema and psychis disturbances were noted in 9 cases. In 4 of these the treatment had to be discontinued.

In 15 of the 36 cases in which the treatment was carried through, there occurred a fall in diastolic blood pressure of between 10 and 19 mm. Hg. and in 2 cases a fall of 20 mm. Hg. or more. In 13 patients the systolic pressure fell by from 20 to 39 mm. Hg., while 7 showed a fall of 40 mm. or more. In 14 cases there was seen a simultaneous fall in systolic and diastolic pressure.

In 24 cases the treatment was continued in ambulatory form. In 20 of these there occurred a slight rise in systolic and diastolic pressure, while in only 4 cases did the diastolic pressure remain at the same level as during treatment in the hospital.

In 12 patients the thiocyanate therapy was discontinued and there then occurred in 6 of them a distinct increase of the systolic and/or diastolic pressure.

The effect on the subjective symptoms, especially the headache, was considerably more pronounced, as 13 patients became quite free from symptoms and 10 showed distinct improvement, while only 9 were entirely unaffected. In 4 cases there was seen for some time a considerable improvement of the symptoms, which, however, recurred in spite of continued treatment.

No correlation was found between the patient's age, the duration of the symptoms, the state of the eye fundus, or the occurrence of cardiac insufficiency and the effect of the thiocyanate treatment on the subjective symptoms and on the blood pressure. On the other hand, the treatment was least effective in patients who had previously had relatively high blood pressure and serious affections of the eye fundus.

No inverse proportionality was noted between the height of the blood pressure and the spontaneous concentration of thiocyanate in serum.

The Clinical Significance of a Deep Q Wave in the Third Lead of the Electrocardiogram. H. LJUNGGREN, Stockholm, Sweden. Acta med. Scandinav. *139*:176-84, f. 1, 1951.

A series of 151 ECG patients with a Pardee Q, 137 without and 14 with posterior infarction, at Serafimerlasarettet from 1938-442 were reviewed. It was found that a deep Q_3 in patients without infarction lacks significance as a reliable sign of clinically important heart disease. So-called unipolar leading from the left leg appears to be valuable for a diagnosis of Q_3 due to infarction.

The Latent and Manifest Reciprocation Mechanism in Lower Atrioventricular Nodal Rhythm Coexistent with Sinoauricular Rhythm. P. FLEISCHMANN, Affula, Israel. Acta Cardiol. *6*:164-89, Feb. 1951.

The case of a young pregnant woman is presented whose heart is simultaneously activated by an S-A and an A-V pacemaker. Their impulses interfere with each other and produce a variety of cycle sequences, which include latent and manifest reciprocal rhythm.

Measurement and statistical evaluation of more than 2,000 cardiac cycles reveal the common nature of both forms of reciprocal rhythm. In both a retrograde impulse ascends from the A-V pacemaker until it reaches a constant level within the A-V node, where the impulse splits; after some delay at this level, the ascending branch of the impulse reaches the auricle, while the reflected branch returns to the pacemaker. The only evidence thereof is the premature discharge of the pacemaker, while the ventricles are still refractory to stimulation (latent reciprocation). Under suitable conditions the reflected impulse re-enters an ascending conduction path, both ascent and reflection are repeated, and the descending impulse activates the ventricles (manifest reciprocation).

In some cycles the reciprocation mechanism is inhibited by suitably timed S-A impulses; in others, the mechanism is protected from inhibition. In latent recipro-

cation, the consequence is a succession of short and long QQ intervals, whole numerical proportion depends on the relation between the S-A and the A-V rate. Under defined conditions, the alternation of short and long intervals leads to a peculiar form of bigeminy.

Since the S-A impulses occur in variable phases of A-V activity, their impact on the reciprocation mechanism probes the node and permits the construction of a substantiated pathway model.

Reciprocal rhythm is due to a single or repeated circus movement of the impulse, whose path is limited to the A-V node. Owing to this location, the successive phases of the impulse revolution can be registered by the ECG. It is suggested that the reciprocal rhythm reveals a preformed structure of the normal atrioventricular node. The reflecting level of the reciprocation mechanism is probably the site of the normal impulse delay, which is characteristic of the node.

Congenital Heart Disease. II. Angiocardiography, Aortography and Cardiac Catheterization. DANIEL F. DOWNING ET AL., Newark, N. J. J. M. Soc. New Jersey *48*:47-50, Feb. 1951.

The technics of cardiac catheterization, angiocardiography and thoracic aortography are briefly discussed. Cardiac catheterization is indicated, in general, in acyanotic lesions in which a left-right shunt is suspected. Angiocardiography is indicated in all cyanotic cases and is of help in the diagnosis of interauricular septal defects in infants. Thoracic aortography should be performed in all cases known to have, or suspected to have, coarctation of the aorta. It is diagnostic in aortic septal defects and is often of aid in the dignosis of atypical patent ductus arteriosus.

Emphasis is played on the early diagnosis of the nature of the lesion in infants with cyanotic congenital cardiac defects. If the condition is amenable to surgery, the operative procedure is then possible as an emergency measure should events prove its necessity. 9 references.—*Author's abstract.*

The Sequence of Circulatory, Respiratory and Cerebral Failure During the Process of Death: Its Relation to Resuscitability. H. G. SWANN AND M. BRUCER, Galveston, Texas. Texas Rep. Biol. & Med. *9*:180-219, Spring 1951.

The sequence of circulatory, respiratory, and cerebral failure was determined during the process of death in dogs. Circulatory failure is the point during the terminal collapse in blood pressure at which periodic insufflation of the lungs with oxygen just fails to restore the circulation. Respiratory failure is the point at which apnea supervenes. Cerebral failure is the point at which an irreversible cerebral insult is done by the anoxic experience. Four types of death were investigated: the fulminating anoxia of breathing pure nitrogen, the acute anoxia of breathing 2.43 per cent O_2 in N_2, carbon monoxide poisoning (one per cent CO), and obstructive asphyxia. The induced anoxia served as the general anesthetic in all experiments.

In fulminating anoxia, O_2 insufflation uniformily succeeded in restoring the circulation when the systolic blood pressure was 105 mm. Hg or greater but uniformly

failed when it declined to 75 mm. or less, with 15 seconds, on the average, elapsing between the two points. Regardless of the time at which the two points appeared, the first point showed when circulatory failure was imminent and the second when it had just occurred.

In fulminating anoxia, the breathing always fails before the circulation, 84 seconds, on the average, elapsing between respiratory and circulatory failure. Respiratory failure could not be clearly related to circulatory failure, regardless of what component of the breathing pattern during the process of death was examined. The cerebrum failed at six and one-half minutes after the onset of fulminating anoxia, the damage being so overwhelming at this time that no dog lived more than two days in spite of careful nursing and artificial feeding. But after five and one-half minutes of exposure, apparently complete recovery of the dogs took place. All dogs in the latter two groups were resuscitated by O_2 insufflation and extrathoracic cardiac massage, because both apnea and circulatory failure had occurred before the overwhelming cerebral insult took place.

In acute anoxia, all dogs were resuscitated with periodic O_2 insufflation, regardless of the duration of the anoxia, when the systolic blood pressure was 90 mm. Hg or greater. But when it declined to 55mm. Hg, the attempt to resuscitate uniformly failed. On the average, 16 seconds elapsed between the two points. The breathing failed sometimes before, sometimes simultaneously with, and sometimes after circulatory failure, the latter phenomen occurring in one third of the cases. No cerebral insult was done if the dogs were resuscitated when just on the threshold of circulatory failure; but an overwhelming cerebral insult, causing death in a few days, was done when the dogs were resuscitated one minute after circulatory failure. This was independent of the duration of the acute anoxia; it was related only to the time of circulatory failure.

In CO poisoning, all dogs were resuscitated with O_2 insufflation when the systolic blood pressure was 100 mm. Hg or greater, but none were resuscitated if the pressure was allowed to fall to 40 mm. On the average, 32 seconds elapsed between the two points. As in acute anoxia, breathing sometimes failed before, sometimes concurrently with, and sometimes definitely after circulatory failure, the latter occurring in one third of the cases. But three quarters of the dogs died 1 to 14 days after the experience, exhibiting typical signs of anoxic decerebration. It is apparent that an overwhelming cerebral insult is usually done in CO anoxia before circulatory and respiratory failure. In many dogs, it was done at a time when the breathing and blood pressure were still very strong.

In obstructive asphyxia, all dogs were resuscitated with O_2 insufflation when the systolic blood pressure was 105 mm. Hg or greater, but none were resuscitated if the pressure had fallen to 45 mm. or less. On the average, 28 seconds elapsed between the two points. Again, breathing movements ceased sometimes before, sometimes at the same time as, and sometimes definitely after circulation failure, the latter phenomenon appearing in one third of the tests. An overwhelming cerebral insult was done by the anoxic experience at three minutes, but not at two minutes, after the onset of circulatory failure.

In none of the four types of death does the pattern of the terminal breathing furnish an exact prediction of circulatory failure. Furthermore, no component of the blood pressure except the systolic gives a sharp prediction of the imminence or fact of circulatory failure; neither the diastolic, nor the pulse, nor the average pressure may be used to define circulatory failure with accuracy.

In round figures, circulatory failure is imminent in all four types of anoxia studied when the systolic blood pressure declines to 100 mm. Hg, and it has actually occurred when the systolic pressure declines to 50 mm; some 20 seconds elapse between the two points. The minimum effective circulation that just permits resuscitation with O_2 is shown to be the one concomitant to a systolic blood pressure of 100, thus suggesting that artificial respiration is futile if the systolic pressure has declined below this point. The data indicate that, in fulminating and acute anoxia and in obstructive asphyxia, the fundamental aim of artificial respiration is to reverse by reoxygenation the process of circulatory failure. The critical circulatory change, uniform for all four types of death, is suggested to be anoxic failure of the myocardium.

It is evident that in dogs the respiration often stops after circulatory failure and not uniformly before, as commonly believed. Only in fulminating anoxia does apnea consistently precede circulatory failure.

An irreversible cerebral insult, caused by the anoxia, takes place in fulminating and acute anoxia and in obstructive asphyxia definitely after circulatory and respiratory failure. But in CO poisoning, it usually precedes circulatory and respiratory failure. Evidence to support the proposition that this often occurs in man is given, with the conclusion that men may need resuscitation when the breathing and blood pressure are still good.

Because the weakest link during the process of death differs with each type of anoxia—now the breathing, now the circulation, and now the cerebrum—it is apparent that the aim of resuscitation also must differ in the several types of anoxic death. 36 references. 11 tables.—*Author's abstract.*

A Simple Method of Measuring the Q-T Ratio. J. E. SMITH, Washington, D. C. M. Ann. District of Columbia *20*:6-8, Jan. 1951.

One of the most difficult problems in utilizing the measurement of the Q-T interval has been variations of the measurement with the actual pulse rate and the effects of respiration on varying the pulse rate. The pulse rate is more variable than the Q-T measurement.

Goldberger found that it is easier to establish a ratio by comparing the ideal Q-T for a given pulse rate with the actual measured Q-T. He used Bazett's formula of $Q\text{-}T = k_2 R\text{-}R$ in which k was 0.40 second. By dividing the ideal Q-T into the measured Q-T a ratio was established and called the Q-T ratio or Q-TR. In measuring large groups of normal hearts, Goldberger found that the average normal was 1.01, but that occasionally apparently normal people can have Q-T ratios as high as 1.08 in children and men and 1.12 in women.

In our work with myocardial strain tests and exercises electrocardiograms, we have established that the resting Q-TR of most normal people is about 1.00; the average

was 0.99 in 100 normals. Also, we established that after a double two-step exercise test the Q-TR drops slightly or remains the same and rarely increases slightly above the resting Q-TR. In some cases of myocardial insufficiency after exercise the Q-T ratio may be markedly prolonged.

Charts have been designed for accurate and simple clinical use.

Q-T ratios between 1.01 and 1.08 must be interpreted with caution, but ratios above 1.08 probably signify definite prolongation of the Q-T interval. It is suggested that the measurement of the Q-T ratio should be a routine measurement of the electrocardiogram. 14 references. 2 figures.—*Author's abstract.*

Alternating Bidirectional Tachycardia. M. E. BERK AND H. GOTSHALK, Honolulu. Hawaii M. J. *10*:186-89, Jan.-Feb. 1951.

This is a case report of a 51 year old Hawaiian who was admitted to the Queen's Hospital (April 1945) because of shortness of breath and ankle swelling. These symptoms antedated his admission by a few weeks. He was given digitalis and discharged. In August 1945, he was readmitted because of congestive heart failure. He was again given digitalis and advised to check regularly with his family physician. In January 1946, he was admitted for the third time because of far advanced congestive heart failure. He had had no digitalis for approximately three months. His rhythm was regular. His ventricular rate was 160; with carotid sinus pressure, the rate dropped to less than 100 but returned to 160 after release of pressure.

Electrocardiograms showed a diphasic alternating tachycardia, which was completely stopped by applying carotid sinus pressure. The tracing done while pressure was applied shows a reversion to a normal rhythm; this tracing resembles those taken in 1945. The positive deflections of the diphasic tachycardia are apparently of nodal origin, and it is our suspicion that the negative deflection arises in the most inferior part of the A-V node. We further assume the impulse is on the left side of the lowest portion of the A-V node, thus influencing the direction of the QRS complex downward. A discussion of other theories, particularly those involving ventricular tachycardia are shown to be not valid.

After 53 months the patient is well compensated and active. Following the administration of digitalis, his auricles began to fibrillate and he has continued in this condition. 5 references. 6 figures.—*Author's abstracts.*

Clinical Measurement of the Electrical Resistance of a Patient. PIERRE JEANNERET, Lausanne, Switzerland, Brit. Heart J. *13*:43-46, Jan. 1951.

Main and variable part of body resistance resides in the skin. Gross electrical resistance and skin capacity influences electrocardiographic leads involving shunts. For this and other reasons, a simple circuit was devised for measuring clinically with an amplifier type of electrocardiograph, the electrical resistance of a patient. This procedure is based on the shunt of a known voltage through the body and no error arises from skin capacity.

Equation $s = \frac{100\,r}{Y} - r\ \Omega$ is used for calculation of the body resistance, where s is the body resistance, r is the internal resistance of the source of voltage used, and Y the percentage drop between the open-circuit voltage "e" and the potential difference "v" at the terminal, of the source connected to the body. Both voltages, before (e) and after shunt across the body (v) are easy to record with an ordinary high input-impedance amplifier cardiograph. The calculations are quick and accessories to the cardiograph are few, consisting only of a dry cell, a voltage divider, and a calibrated resistance. No artefacts arise from the skin capacity. This is discussed in the original paper. 17 references. 2 figures.—*Author's abstract.*

Myocardial Injury at Cardiac Catherization. Report of a Case. G. BIORCK & H. KROOK, MALMO, Sweden. Acta Cardiol. *6*:101-106. Feb., 1951.

Electrocardiograms and intracavity pressure recordings from the cardiac catherization of a boy with patent ductus Botalli and pulmonary stenosis are presented. Whereas disturbances of impulse formation and conductivity are observed alternating with normal findings during the whole procedure, at catherization of the right ventricle additional features appear, i.e., signs of marked subendocardial injury together with marked reduction of right ventricular systolic pressures. These disturbances have most likely been mechanically induced by the catheter.

Cardiac Evaluation in Combined Respiratory Vascular Disease. B. N. MILLER, Columbia, S. C. J. South Carolina M. A. *47*:57-62, Feb., 1951.

In the patient with a chronic respiratory disease, it is important to evaluate from time to time the proportionate role played by the lungs and the heart in the resultant aeration failure. The interest of the paper is focused on a discussion of this problem, with special emphasis on practical methods to be used in assaying these two factors in the following group of cases: (1) asthmatic emphysematous patients with evolving right-sided heart failure (cor pulmonale); (2) asthmatic emphysematous patients with heart disease other than cor pulmonale (primary heart disease); (3) problems in differential diagnosis between (a) left-sided failure with degrees of pulmonary edema, with and without paroxysms of cardiac asthma, (b) inflammatory lung disease, and (c) bronchial asthma.

The detailed study of the cardiac silhouette, ECG, venous pressure, circulation time, and vital capacity in cardiorespiratory problems will clarify in a revealing way the mechanism involved in individual cases. This in turn will allow for more exact prognosis and properly directed treatment. Individual heart chamber enlargement reflects the burden of work load. The ECG will record hypertrophy and strain patterns. In right-sided heart failure evolving from chronic lung pathology, there is a relatively early increase in systematic venous pressure; this is particularly evident in response to exercise. The circulation time is not proportionately increased. This is in contrast to primary left-sided failure where back pressure pulmonary

hypertension and consequent right-sided failure must precede any increase in systemic venous pressure. Consequently, there is an early increase in circulation time and a delayed increase in systemic venous pressure in primary left-sided heart failure. 10 references.—*Author's abstract.*

Stenosis of the Pulmonary Conus Without Associated Defects: A Case Report. ERNEST O. THEILEN AND LEWIS E. JANUARY, Iowa City, Iowa. J. Iowa M. Soc. *41*:88-91, March 1951.

A case of stenosis of the pulmonary conus of the right ventricle at the lower orifice as the sole demonstrable cardic anomaly in a 48 year old man is presented. The mechanism of the production of the associated murmurs is considered. The case was complicated by a superimposed subacute bacterial endocarditis with probable origin in an infected pilonidal sinus. A possible explanation for the unexpected sudden death is offered. 6 references. 2 figures.—*Author's abstract.*

The Use of Anticoagulants in Military Medicine. I. S. WRIGHT, New York. Mil. Surg. *108*:113-15, Feb. 1951.

The Army population is subject to all of the cardiovascular illnesses and accidents of civilian life and, in addition, those which may arise from the hazards of military life. The loss of manpower and permanent disability from thrombo-embolic diseases in World War II is estimated at the equivalent of several divisions.

The use of anticoagulants in the treatment of thrombo-embolic conditions is now well established. Every Army installation which takes care of thrombo-embolic cases should be equipped to provide correct anticoagulant therapy. This is best provided for in terms of a team responsible for this aspect of treatment. Heparin and dicumarol have been the anticoagulants which have been used most widely in the past. Tromexan, another coumarin derivative, has now proved to be an advance in anticoagulant therapy. It acts more rapidly than dicumarol and its action ceases more quickly than dicumarol. These drugs must be used with skill and by physicians who are impressed with the necessity for meticulous observation of the patient.

A full exploitation of available knowledge in this field will result in a striking reduction in the incidence of death and complications in the thrombo-embolic and vascular conditions commonly encountered in military life.—*Author's abstract.*

Diagnosis of Aortic Stenosis. Based on a Study of 25 Proved Cases. DAVID LEWES, London, England. Brit. M. J. No. *4700*:211-16, Feb. 3, 1951.

Aortic stenosis is an important clinical entity, but the frequent failure to diagnose the condition in life is due to the demand for too rigid diagnostic criteria by clinicians as well as lack of familiarity with the natural history of the disease.

In a series of 2,245 routine necropsies, significant aortic stenosis was found in 1.8 per cent of cases. Calcareous aortic stenosis, as the sole valvular lesion was present in 25 cases (1 per cent of total necropsies). In these 25 cases, which were submitted to a detailed retrospective clinical analysis, the commonest causes of

death were heart failure and infective endocarditis. In only 3 cases was aortic stenosis an incidental postmortem finding. Twenty-two patients first came under medical observation because of cardiac or cerebral symptoms due to their valvular lesion. Males were affected three times as often as females; symptoms did not usually appear until the sixth or seventh decade, and a history of past rheumatism was exceptional. The commonest presenting symptoms were exertional or nocturnal dyspnea, cardiac pain, syncope, and giddiness. The average survival following the first symptom was 14 months. Patients rarely survived a second attack of acute heart failure, which was strikingly resistant to treatment and commonly accompanied by mental confusion, epileptiform convulsions, maniacal violence, and drenching sweats. Sudden or unexpected death was a common termination.

A correct clinical diagnosis was made in 13 of the 25 cases, but on the bases of the classic signs of an aortic systolic murmur and thrill, absent aortic second sound, and a small pulse, less than one sixth of the cases would have been recognized clinically. Correct clinical diagnosis was made in all 5 cases of severe stenosis, but in only 6 of moderate and 2 of mild valvular narrowing was the clinical impression correct.

A small pulse was noted in under half and auricular fibrillation in one fifth of the cases. Displacement of the apex beat was usual. An aortic systolic basal thrill was noted in 9 cases, but in 4 a systolic thrill at the *mitral* area was also recorded. Harsh aortic systolic murmurs were nearly always accompanied by a similar murmur in the mitral area. In 6 cases the murmur was loudest at the apex. In a fifth of the series the systolic murmur was widespread. Aortic diastolic murmurs were recorded in half the cases. Absence of the aortic second sound was a useful but uncommon finding. Persistent triple heart rhythm was noted in 4 cases. Blood pressure readings were of value in diagnosis, and hypertensive figures were usually an accompaniment of acute left ventricular failure.

Radiology showed left ventricular enlargement in all but 7 cases, but the classic radiologic appearances of aortic stenosis were invariably obscured by aortic unfolding or generalized cardiac enlargement due to congestive heart failure.

Electrocardiography was only of value in elucidating rhythm disorders and conduction defects which were frequent. Left bundle branch block was found in one fifth of the cases.

Calcification of the aortic valve was observed in life in only 2 out of 5 cases in which it was sought and was seen only by fluoroscopy. Since calcification of the valve was present in every case in the series at postmortem, fluoroscopy during life could have reversed an incorrect clinical diagnosis in 6 cases in which subsequent autopsy calcification was found to be gross. Although correct diagnosis was made on the basis of a harsh aortic systolic murmur in 4 other cases, a more careful evaluation of the site and character of systolic murmurs should have led to a higher proportion of correct clinical diagnoses in the series. Closer attention to the characteristic course of the illness after the onset of symptoms, coupled with the ausculatory findings, should likewise have permitted a higher proportion of correct clinical diagnoses. 25 references. 5 tables.—*Author's abstract.*

Diagnosis and Treatment of Chronic Occlusive Disease of the Peripheral Arteries. NELSON W. BARKER, Rochester, Minn. Journal-Lancet *71*:58-62, Feb. 1951.

The diagnosis of chronic occlusive disease of the peripheral arteries is not difficult if the physician has a high threshold of suspicion for its presence when patients have pain, ulceration, gangrene, changes in temperature, or discoloration in an extremity. The most important physical sign is impairment of pulsations in the peripheral arteries. Postural color changes are a good rough indication of the degree of ischemia. There are two important chronic occlusive peripheral arterial diseases, thromboangiitis obliterans and arteriosclerosis obliterans, and almost always they can be distinguished clinically. The general principles of treatment can be classified under the broad headings of: (1) efforts to arrest the progress of the disease, (2) procedures to produce dilatation of uninvolved arteries and arterioles, (3) efforts to increase circulation by mechanical means, (4) procedures for direct relief of pain, (5) instruction in prophylaxis against injury of ischemic tissues, and (6) treatment of ulceration and gangrene. 7 tables.—*Author's abstract.*

The Eisenmenger Complex and Its Relation to the Uncomplicated Defect of the Ventricular Septum. ARTHUR SELZER, AND GERT L. LAQUEUR, San Francisco, Calif. Arch. Int. Med. *87*:218-41, Feb. 1951.

Two new cases of the Eisenmenger complex in adults are reported in detail. In addition, data on 33 autopsied cases of this syndrome are tabulated and their clinical and pathologic features reviewed. Following the lead of Saphir and Lev, the concept of the Eisenmenger complex is widened to include cases in which the aorta is completely dextroposed, arising from the right ventricle.

Clinical features of the Eisenmenger complex include cyanosis, which is frequently present from birth; noncharacteristic systolic and diastolic murmurs with a loud pulmonary second sound; roentgenologic evidence of striking dilatation of the pulmonary artery and its branches associated with pulmonary congestion and increased arterial pulsations and evidence of right ventricular enlargement and hypertrophy in the roentgenogram and electrocardiogram.

Pathologic features of the Eisenmenger complex include a localized high defect of the ventricular septum, usually oval or crescentic, measuring between 1 and 2.5 cm. in longest diameter; varying degrees of dextroposition of the aorta, from minimal over-riding to a complete origin of the aorta from the right ventricle; dilatation of the pulmonary artery and its branches, and severe hypertrophy of the right ventricle, with or without some left ventricular hypertrophy.

Microscopic examination of the pulmonary arterioles in our 2 cases revealed severte intimal and medial changes. Such changes also have been noted by others, and it is believed that they constitute a characteristic feature of the Eisenmenger complex, being evidence of long-standing severe pulmonary hypertension.

Further evidence is presented to support the view that no dividing line exists between the uncomplicated defect of the ventricular septum and the Ensenmenger complex and both are caused by varying degrees of the same process of maldevelop-

ment. The distinguishing feature of the two syndromes—the dextroposition of the aorta—may be difficult to determine owing to the fact that, in the absence of the membranous septum, there is a physiologic over-riding of the aorta and that an examination of the specimen of the heart may not permit an estimate of the degree of dextroposition which existed during life. It is believed, also, that the degree of over-riding may be subject to change during a patient's lifetime.

The pathogenesis of cyanosis associated with the Eisenmenger complex is discussed. Evidence is presented that anoxemia and cyanosis are due to admixture of venous blood in the aorta or the shunt mechanism rather than to incomplete pulmonary oxygenation.

The hemodynamics of the Eisenmenger complex are presented in the light of recent measurements of intracardiac pressure. Severe pulmonary hypertension has always been recorded, and in the majority of cases equalization of pressure in the systemic and pulmonary circulation was established. This feature is discussed in connection with the concept of the "double outlet ventricle," in which it is postulated that equal resistance offered by the pulmonary and systemic arterioles is essential for survival and has to be present from birth.

Four cases are included in which the triad of basal defect of the ventricular septum, dextroposition of the aorta, and deformity of an aortic cusp causing aortic insufficiency existed. In contrast to the remainder of the series, in 3 of these cases cyanosis was absent, and in the fourth, it was questionable. It is thought that because of the associated aortic lesion the dextroposition of the aorta was nonfunctioning, and therefore it is suggested that these cases be classified as ventricular septal defects and not as Eisenmenger's complex associated with aortic insufficiency. The Ensenmenger complex is redefined by a combined pathologic and physiologic set of criteria. 25 references. 9 figures, 3 tables.—*Author's abstract.*

Quinidine Sulfate in Propylene Glycol by Intramuscular Injection in Man. J. L. GLUCK, H. GOLD, T. GREINER, W. MODELL, N. T. KWIT, S. THICKMAN, H. L. OTTO, AND L. J. WARSHAW, New York, N. Y. J.A.M.A. *145*:637-40, March 3, 1951.

There is need for a satisfactory preparation of quinidine for intramuscular injection in the treatment of disorders of cardiac rhythm because, in many patients, the local irritant action of quinidine in the gastrointestinal tract causing pain, nausea and vomiting, and especially diarrhea, is a bar to the use of sufficiently large doses to bring the ectopic rhythm under control. When the oral route is not possible, intravenous administration is usually substituted, but there are risks in the intravenous use of quinidine in cardiac disorders.

A 20 per cent solution of quinidine sulfate in propylene glycol (prepared by Marvin R. Thompson, Inc., of New York) was tested for its local irritant effects by intramuscular injection in 19 patients, and in 7 of these it was tested for its action on the auricle in auricular fibrillation and flutter.

The results show that a single dose of this preparation by intramuscular injection produces negligible local reactions at the site of injection. It produces either no pain or pain of varying intensity but almost invariably of very short duration. In

2 of 3 patients who received 12 or more injections at intervals of 3 to 6 hours some swelling of the soft tissues occurred. It subsided gradually and was not associated with pain, redness, induration, or slough.

The curve of action of quinidine given by intramuscular injection in the form of this preparation is essentially similar to that by oral administration, the peak effect being reached in an average of about three hours, about half of the effect wearing off in about eight hours, and the effect disappearing completely in 24 hours or less.

Observations were made showing that, by suitable dosage regimens of intramuscular injections of this preparation, effective concentrations of quinidine may be maintained for protracted periods.

Quinidine sulfate in propylene glycol by intramuscular injection meets an important need in quinidine therapy. It is especially applicable to certain kinds of cases: (1) those in which the oral administration gives rise to diarrhea or other gastrointestinal symptoms, (2) patients in coma, (3) for the prevention and treatment of disorders of heart rhythm during surgery and anesthesia. 6 references. 5 figures. 2 tables.—*Author's abstract.*

GENITOURINARY DISORDERS AND DISEASES

Estrogen and Alkaline Phosphatase Activity in the Genital Tract of the Male Mouse. H. A. BERN, Berkeley, Calif. Endocrinology *48*:25-33, Jan. 1951.

Castration of male mice results in partial disappearance of stromal alkaline phosphatase activity from the vas deferens, seminal vesicle, and anterior and dorsal prostates. Retention of phosphatase occurs in the subepithelial stroma of the vas and seminal vesicle, where activity seems to be relatively independent of testicular androgen. Estrogen administration maintains the normal localization of stromal alkaline phosphatase in the latter organs of castrates and thus may substitute for androgen in these areas.

Squamous metaplasia, including keratinization, occurs extensively in the anterior prostate and, to a limited extent, in the dorsal prostate and seminal vesicle. The intensely alkaline phosphatase-active replacing epithelium, first evidenced as proliferating basal cells, stands out in sharp contrast to the inactive original epithelium. In this process, the alkaline phosphatase activity serves almost as a differential stain. 34 references. 10 figures, 2 tables.—*Author's abstract.*

GASTROINTESTINAL DISORDERS AND DISEASES

Measurement of Serum Cholinesterase Activity: A Useful Test in the Management of Acute Hepatitis. LOUIS J. VORHAUS, Chicago, Ill. Am. J. M. Sc. *221*:140-48, Feb. 1951.

When treating patients ill with acute hepatitis, the physician must decide at what point the patient is ready to return to an active life. The problem is far from academic, for it has been demonstrated that the likelihood of developing complications are increased considerably by allowing patients to return to normal activity

too soon in convalescence. The physician's decision cannot be based purely on clinical considerations because, following the subsidence of clinical symptoms and signs of liver disease, there remains a period of smoldering activity which can be detected only by finding disturbed tests of liver function. The question arises as to which of the multitude of liver function tests is most reliable and of greatest help to the physician in deciding when his patient is fit to return to work. In previous communications the authors have shown that the cholinesterase activity of the serum is almost invariably depressed in patients ill with hepatocellular disease, and they have reported that serial studies of serum cholinesterase activity are most valuable as a guide to the changing status of hepatocellular function in patients ill with chronic disease of the liver. This communication reports observations in 7 patients ill with acute liver disease. In them, serial changes in serum cholinesterase activity were compared with changing clinical status and with serial changes in 10 commonly used liver function tests. Serum cholinesterase determinations were performed by Michel's electrometric method, a simple and accurate technic. In all patients, the serum cholinesterase activity was low initially, and in every instance there was a sharp rise in serum cholinesterase activity during recovery. Four patients showed evidence of one or more mild and generally subclinical remissions during the course of their recovery. In every case the serum cholinesterase activity dropped temporarily during the relapse. When compared with the 10 other liver function tests which were carried out, it reflected the patients' changing condition sensitively and with greater uniformity and regularity than any other test. It is concluded that measurements of serum cholinesterase activity are of great value to the physician in following the course of the patient ill with acute liver disease. 35 references. 2 figures. 7 tables.—*Author's abstract.*

Observations on the Epidemiology of Infectious Hepatitis. EDNA M. CREE, Madison, Wisc. J. Lab. & Clin. Med. *37*:104-21, Jan. 1951.

This report is concerned with observations which were made on the occurrence of infectious hepatitis in two widely separated areas in Wisconsin. The two regions are 221 miles apart and presented obvious differences in social, environmental, and geographic aspects. The populations have remained static for a number of years.

In each locality, a few cases of infectious hepatitis of recent occurrence were discovered.

The occurrence of infectious hepatitis in the two localities in Wisconsin did not constitute an epidemic. In both, the disease involved relatively few individuals over a period of several months. The most interesting features of this study seem to consist of the tendency of the disease to occur and remain localized in families and to present a limited geographic distribution without regard to other influences, so far as could be determined. The observations demonstrated that there was opportunity for contact transmission of the infection in nearly every case. The opportunity was also present for dissemination of diseases by the gastro-intestinal route. A review of the data accumulated did not provide conclusive support for the theories of either direct contact, air-borne, or water-borne transmission. Serum transmission might

be important. It does not seem necessary to limit the considerations to the use of the hypodermic needle. Other methods of transmission, not heretofore considered, should be sought in the attempt to explain the natural dissemination of this disease. Continued observations in the field are important to the ultimate solution of this problem. 9 references. 7 figures, 4 tables.—*Author's abstract.*

Use of Radioactive Tracer Material in the Differential Diagnosis of Experimental Jaundice. WALTER W. CARROLL, Chicago, Ill. Quart. Bull., Northwestern Univ. M. School *25*:13-8, Spring 1951.

The differential diagnosis of clinical jaundice long has been a problem common to all physicians. Since the usual clinical laboratory test used for the solution of this problem has concerned itself with hepatic function, it seemed interesting to the authors to investigate the metabolism of one of the dyes which has been shown to be excreted largely by the liver, using the radioisotopic tracer technic.

After an efficient method for synthesis of radio-active tetraiodophenolphthalein of high biologic purity was accomplished, this substance was injected intravenously into 40 female dogs. Multiple determinations were then done on various samples of blood, urine and feces. The conclusions drawn were: 1. Following the intravenous administration of radioactive tetraiodophenolphthalein, predictable blood and urinary dye levels can be obtained in the normal dog. 2. When the common bile duct is completely obstructed by ligature, alterations in these blood and urinary dye level curves occur which are diagnostic. 3. When the liver suffers acute cellular necrosis, such as is produced by controlled chloroform intoxication, the resultant jaundice can be differentiated from that due to common duct obstruction by predictable alterations in these same dye level values. 4. Detailed analysis of renal excretion date during the first 12 hours of this test served further to differentiate between the normal and jaundiced dogs of the categories described. 5. Stool examinations, although not accurate, served to substantiate these same findings. While certain details necessitating further animal experimentation seemed indicated to clarify more completely the biochemistry and biophysiology of this tracer material, the authors felt that their results were such that the work should be extended to the human subject. 5 references. 4 figures.—*Author's abstract.*

The Insulin Tolerance Test in Cirrhosis of the Liver. S. O. WAIFE, L. O. BRENNER, AND C. M. THOMPSON, Philadelphia, Pa. Gastroenterology *17*:236-41, Feb. 1951.

Since the damaged liver in cirrhosis is partially depleted of glycogen, a study was made of the glycemic response to a small dose of insulin which might test the liver's ability to maintain normal blood sugar levels.

This standard insulin tolerance test was performed on 16 patients with advanced cirrhosis of the liver. Venous blood was drawn at periodic intervals following an overnight fast. Four patients with psychosis were similarly studied and 7 general ward patients convalescing from various medical diseases, but who had no liver impairment, served as controls. The test was also performed on a normal young

female after a 20 hour fast and again 20 hours later while she remained active and without food. According to the accepted normal curve, the insulin tolerance test in cirrhosis showed insulin resistance and some degree of hypoglycemic unresponsiveness. The blood sugar did not fall as far or as rapidly in the cirrhotics as in the controls and did not return to normal levels within two hours. The 4 psychotic patients showed normal insulin sensitivity by hypoglycemic unresponsiveness. The noncirrhotic controls had an essentially normal curve. The cirrhotic type of curve was found after a 40 hour fast, in comparison to the normal curve found after a 20 hour fast, in the young healthy subject.

The various neuro-endocrine and metabolic features of the response of blood sugar to insulin is discussed. It is suggested that the insulin resistance of cirrhotics may be due to what is essentially a state of starvation because of impaired utilization of food stuff, even in the presence of an adequate oral intake. 14 references. 3 figures. 1 table.—*Author's abstract.*

The Ether Test and Its Applicability in the Differential Diagnosis of Jaundice. E. NINGER AND J. TOVAREK, Brno, Czechoslovakia. Acta med. Scandinav. *139*:242-43, f. 1, 1951.

The ether test, which had been repeatedly recommended for the diagnosis of cancer in jaundiced patients, was examined on a controlled series of patients. Sera of patients with all kinds of jaundice gave both positive and negative results, so that this test could not be used as a diagnostic aid in jaundice.

The Use of the Laboratory in the Diagnosis of Liver Disease. T. J. RANKIN, Wichita, Kan. J. Kansas M. Soc. *52*:53-58, Feb. 1951.

A clinically useful group of laboratory tests in hepatic disease can be chosen from the many used and proposed in the literature. The spread of tests must be of fair number and of varying selective range. Any single test can be positive because of disturbed physiology elsewhere than in the liver or, conversely, can be negative in the presence of liver disease.

The functioning unit within the liver is a combination of liver cell and endothelial sinusoidal lining between the sinusoidal blood and the biliary canaliculus. Biliary excretion, alteration of metabolites, and metabolic storage are accomplished within this microanatomic area. Inflammation in this area as in hepatitis, disturbance of cellular function with periportal infiltration and fibrosis as in cirrhosis, and disruption of structure and function from back pressure of extrahepatic obstruction are among the pathologic entitles reducing liver function.

Liver tests chosen should be readily susceptible to determination by a good clinical laboratory, readily comparable within the literature on hepatic disease and have a practical range of sensitivity. The excretory tests chosen are: urinary bile, one minute (direct) and total minus one minute (indirect) serum bilirubin, urinary urobilinogen present in the two hour afternoon specimen, and bromsulfalein tolerance

determined 45 minutes following a dose of 5 mg./Kg. of body weight. The metabolic tests chosen are: thymol turbidity, cephalin flocculation, cholesterol esters in a percentage of total cholesterol, serum albumin and globulin, prothrombin time in a percentage of normal with determination after administration of Vitamin K when indicated, and the five hour oral glucose tolerance test. The author believes the inclusion of the glucose tolerance test in an hepatogram a very sensitive addition. That it can be disturbed by disease other than in the liver only calls attention to this truth of all hepatic laboratory procedure. Alkaline phosphatase and total cholesterol are added as useful in the differential diagnosis of jaundice when the bromsulfalein determination is omitted.

These tests are arranged in an hepatogram of four groups:

Group 1.—Urinary bile, serum bilirubin, urinary urobilinogen, thymol turbidity, cephalin flocculation, and bromsulfalein tolerance. It is considered sensitive and constitutes a good diagnostic group or screening section.

Group 2.—Cholesterol ester percentage of total and glucose tolerance. This is also sensitive and constitutes further laboratory confirmation, when positive, or positive findings in Group 1.

Group 3.—Serum albumin and globulin and prothrombin time. This is less sensitive and constitutes, when positive, an indication of more extensive liver damage.

Group 4.—Alkaline phosphatase and total cholesterol. This is applied to the study of jaundice where metabolic tests are normal and excretory tests are positive. Alkaline phosphatase, particularly, is high in obstructive jaundice or cholangiolar damage in hepatitis.

This hepatogram is more useful in following the progress of hepatic disease than in diagnosis. Group 1, then Group 2, then Group 3 become positive as laboratory evidence of hepatic damage becomes greater. With recovery, positive laboratory tests usually recede in reverse order. However, the vagaries of laboratory determination in liver disease offer many exceptions. The author wishes to suggest this group of laboratory tests in liver disease as a useful one and applicable in the good clinical laboratory. In no sense is the laboratory to be considered a substitute for proper clinical evaluation and acumen. 14 references. 6 figures. 1 chart.—*Author's abstract.*

The Bromsulfalein Liver Function Test With Special Reference to Renal Excretion. JOHN W. NORCROSS, Boston, Mass. Am. J. M. Sc. *221*:137-39, Feb. 1951.

Rosenthal and White introduced the bromsulfalein test for liver function in 1924. Ingelfinger et al reported 10 per cent urinary excretion in two hours of 10 per cent following a 5 mg. per Kg. dose in patients with severe hepatic disease.

Results in the current study after 5 mg. per Kg. dose of bromsulfalein showed:

1. Thirty normal controls with blood retention after 40 minutes of 0 to 5 per cent excreted 0.2 to 1.9 per cent, averaging 1.1.

2. Sixty-seven tests on 60 patients with 0 to 5 per cent retention at 40 minutes excreted 0.04 to 3.5 per cent, averaging 1.2 per cent.

3. Fifty-six tests on 48 patients retaining 6 to 20 per cent at 40 minutes excreted 0.14 to 6.9 per cent, averaging 1.8 per cent.

4. Nineteen tests on 17 patients retaining 20 to 80 per cent at 40 minutes excreted 0.7 to 9.8 per cent, averaging 2.7 per cent.

Degree of bromsulfalein retention did not correlate with quantity of urinary excretion. The maximal renal excretion occurs in 10 to 20 minutes following injection. Blood retentions were not significantly altered by renal excretion.

Conclusion: Although urinary bromsulfalein excretion does not significantly affect liver function results, it may be an important source of error in studies of hepatic blood flow in patients with abnormally high blood retentions. 4 references. 1 figure. 1 table.—*Author's abstract.*

Chronic Renal Disease with Secondary Hyperparathyroidism. D. G. B. RICHARDS, Birmingham, England. Brit. M. J. No. 4699:167-69. Jan. 27, 1951.

Long-standing renal insufficiency may lead to parathyroid hyperfunction and hyperplasia. In some cases calcium salts may be deposited in the arterial tree and other tissues (metastatic calcification), while in a few instances bone lesions, similar in every respect to the osteitis fibrosa of primary hyperparathyroidism, may occur.

A case is reported of a 44 year old woman who suffered from long-standing renal insufficiency due to chronic nephritis. She had gangrene of the toes of one foot, due to occlusive vascular disease. Roentgenograms showed widespread calcification of the arterial tree, and a skull x-ray showed marked osteoporosis.

On postmortem examination the arteries showed advanced medial and intimal degeneration, with heavy calcification. The mitral and aortic valves were calcified, and there was massive calcification of the bronchial cartilages. The skull was thickened and soft, and histologically the bones showed lacunar resorption by osteoclasts and fibrosis typical of classical osteitis fibrosa.

Four large parathyroid glands were found. Three were imbedded in the substance of the thyroid gland (estimated weights, 382 mg., 195 mg., and 221 mg., respectively); one was in its normal position and weighed 419 milligrams. The histology corresponded with Gilmour's type IV. The kidneys were extremely small and histologically the appearance conformed with nephritis repens type II (Russell 1929).

In this case of renal hyperparathyroidism there was marked phosphorus retention (inorganic phosphate 8.7 mg. per 100 ml.), but the serum calcium was normal until just before death. A suggested mechanism for the deposition of calcium salts in the tissues is described. 13 references.—*Author's abstract.*

Observations on Portal Cirrhosis with Ascites. WILLIAM E. RICKETTS, Chicago, Ill. Ann. Int. Med. *34*:37-60, Jan. 1951.

In 50 patients with untreated portal cirrhosis without cardiorenal disease the total plasma proteins, albumin, and globulin were studied before management. The values of the total proteins and globumins showed considerable overlapping in cases with and without ascites. Plasma albumin levels in patients with ascites were below 3 Gm. per cent, while those of normal persons and patients with cirrhosis but without ascites exceeded this figure.

The effect of medical management on the concentration of plasma proteins, on ascites, and on the course of the disease were evaluated. The principles of therapy followed were: to avoid further injury to the liver by toxins such as alcohol; to promote regeneration of the hepatic parenchyma; to improve the general condition of the patient; and to correct the tendency to retention of water and salt in the body. The results of medical management were studied in two groups of patients with ascites: the first 14 cases with jaundice and severe hepatic failure; the second 13 cases without failure or jaundice.

The following conclusions were drawn: (1) The medical management of patients with and without ascites is similar except for sodium retention in patients with ascites. (2) Fluid retention can be controlled by restricting the intake of sodium. (3) Dietary management with a high protein, high carbohydrate, and high caloric intake, plus additional choline chloride, tends to improve nutrition and hepatic parenchymal regeneration, to bring about sustained rise in plasma albumin, and thus to eliminate edema and ascites. This effect is obtained after continuous treatment for several months. (4) Plasma albumin values apparently can be restored only after repletion of tissue protein. (5) Repeated paracenteses should be avoided, since they result in a marked loss of protein. (6) No tendency to recurrence of ascites is seen in uncomplicated cases maintained on an adequate nutrition. (7) The immediate prognosis of jaundiced patients with ascites depends on the severity of the parenchymal failure. (8) The ultimate prognosis of patients who have recovered from edema and ascites remains guarded and is determined to a great extent by the incidence of the complications, the most frequent of which is bleeding from varicose veins of the esophagus. 65 references. 13 figures. 1 table.—*Author's abstract.*

Perforated Peptic Ulcers. WM. H. TOUSEY, Spokane, Wash. Northwest Med. *50*:95-97, Feb. 1951.

In recent years, considerable controversy has arisen as to whether perforated peptic ulcers should be treated in a radical or conservative manner. Anatomic and physiologic classification has been differentiated into acute, subacute, and chronic.

Acute perforation presents a picture of intense agonizing upper abdominal pain, frequently without previous history of gastric distress. However, there are certain general considerations which must always receive careful scrutiny:

The time interval between perforation and operation; electrolytic fluid balance—can be restored before or during surgery; choice of anesthetic—depends on availability of competent administration and surgeon's preference; question of incision—determined by the judgment and experience of the operator; choice of operative procedure—must await exploration of the abdomen after consideration of the patient's general condition.

In addition to the more popular procedures of simple closure and subtotal gastric resection for acute perforated peptic ulcers, some workers have advocated such procedures as gastro-enterostomy, gastrostomy, pylorplasty, simple excision, and primary closure of the ulcer area. The great majority of present-day surgeons, however, prefer to consider of primary importance the saving of the patient's life by a simple closure

of the perforation, reserving a more formidable radical treatment for those patients in whom the following conditions are encountered: perforated carcinoma of the stomach with a resectable lesion; perforated ulcer with simultaneous or recent gross hemorrhage; perforated ulcer with pyloric obstruction; recent perforation in a young individual with a long history of peptic ulcer with poor cooperation but in good surgical condition.

Most surgeons have established definite routine methods for closure. I believe the best method is that which requires less trauma and time, whether it is a suture through the bowel, a plug of omentum, or a combination of both.

In reporting 25 cases, ages ranging from 19 to 67 years, 1 female and 24 males, 15 gave histories suggestive of peptic ulcer; of these 15, 3 were hospitalized and on strict medical management at the time of perforation. Of the 25 cases, 21 were subjected to roentgen film, and free air was reported in all 21 cases. Postoperative complications consisted of one evisceration occurring on the tenth postoperative day in a 64 year old male. Repeated postoperative hemorrhage was observed in only 1 case which occurred two months after operation; while bilateral epididymitis occurred in 1 patient. A 67 year old white male expired from cardiac complications on the sixteenth postoperative day.

The surgeon should always remember that peptic ulcers always will remain primarily a problem of medical management, and the family physician or internist shall be the one who shall effect a cure in this condition much more frequently than those who deal only with the complications.—*Author's abstract.*

An Experimental and Preliminary Clinical Study of the Effect of a New Quaternary Amine, Banthine, upon the Human Colon. F. KERN, JR., T. P. ALMY, AND N. J. STOLK, New York, N. Y. Gastroenterology *17*:198-208, Feb. 1951.

Banthine, a potent anticholinergic agent, is known to inhibit motility of all portions of the resting gastro-intestinal tract. Using the baloon-kymograph technic, we have studied its effect on experimentally induced hypermotility of the sigmoid colon of intact man. The oral administration of 100 mg. of the drug prevents the hypermotility of the sigmoid, which usually follows the ingestion of food, and which follows subcutaneously administered urecholine or morphine sulphate. However, it only partially suppresses the sigmoid hypermotility accompanying emotional tension during a disturbing interview. A preliminary clinical trial of banthine in patients with disorders of intestinal function suggests that it is a useful adjunct in the therapy of some patients with diarrhea or intestinal pain, but it does not affect constipation.

The limited clinical success with this agent is not surprising in the light of its inability to antagonize completely the sigmoid hypermotility of stress and emotional conflict as it occurs in the laboratory. Because of the correlation between laboratory and clinical findings, this simple laboratory technic seems to be a practical method of evaluation of drugs affecting intestinal function.

Despite the apparent limitations of banthine, its potency, as observed in the laboratory and in the clinic, is greater than that of any previously available antispasmodic. 25 references. 5 figures. 1 table.—*Author's abstract.*

Evaluation of Pancreatic Function Tests. C. WILMER WIRTS AND WILLIAM J. SNAPE, Philadelphia, Pa. J.A.M.A. *145*:876-79, March 1951.

The available methods of testing pancreatic function have been reviewed. The fasting serum amylase level is generally considered a satisfactory method of studying acute pancreatitis. In advanced disease the alteration in the character of the stool and glucose metabolism are diagnostic aids. The secretion test is a more accurate method of determining pancreatic function, but it has the serious drawbacks of being too cumbersome, time-consuming and expensive. On the other hand, a study of the serum enzymes after pancreatic stimulation (secretin-morphine) is a simplified procedure that merits further study.

There is suggestive evidence that urecholine increases the level of blood amylase by simultaneously constricting the ampullary mechanism and stimulating enzyme production. Urecholine given subcutaneously to a dog produces a rise in serum amylase similar to that found in the human. However, if the ampulla is made patent by a glass cannula, the serum amylase does not rise significantly in response to the injection. The juice collected from a cannula after urecholine injection is of high specific gravity, indicating increased enzyme content. 27 references. 3 figures.—*Author's abstract.*

Are Achlorhydria, Achylia Gastrica and Pernicious Anemia Precancerous Conditions? FREDERICK S. WEINBERG, New York, N. Y. Am. J. Digest. Dis. *18*:45-52, Feb. 1951.

Increase in the combination of pernicious anemia and cancer of the stomach has been described in the last 15 to 20 years in contrast to the previous rarity of this coincidence.

Chronic atrophic gastritis has been thought a common link between the two diseases, this chronic gastritis in turn leading to achlorhydria or achylia gastrica, which have previously been considered synonymous. This link does not exist. In pernicious anemia found in some statistics has two possible explanations: (1) prolongation of gastric secretion, disturbance of chymification and motility. There is no gastritis. The mucosa can be normal up to degenerative atrophy of fundus and corpus glands. The pyloric region is always free from pathologic changes. In achlorhydria, as it is found in a certain percentage of cancer of the stomach, we have pangastritis.

Achylia gastrica and pernicious anemia have no connection with cancer of the stomach; they cannot be considered precancerous conditions.

It has never been proved whether chronic atrophic gastritis, which leads to achlorhydria, is primary or secondary to gastric cancer. It has been shown, however, that over 80 per cent of all persons in the cancer age have the same gastritic changes as have been found in stomach cancer; these changes are called "physiologic gastritis of old age" and cannot, therefore, be the basis for the development of malignancy.

The increase in frequency of cancer of the stomach in the course of pernicious anemia found in some statistics has two possible explanations: (1) prolongation of life in pernicious anemia due to liver therapy, (2) a carcinogenic agent in the liver. 132 references.—*Author's abstract.*

Differential Diagnosis of Diarrhea. GEORGE K. WHARTON, Los Angeles, Calif. Ann. West. Med. & Surg. 5:59-62, Jan. 1951.

Diarrhea is only a symptom. The differential diagnosis depends on an adequate and complete history and physical examination. Essential procedures are: sigmoidoscopic examination; stools for blood, pus and parasites; and occasionally stool cultures. In the chronic diarrheas, unless the diagnosis is completed with the findings of the barium enema, roentgenologic studies of the entire gastro-intestinal tract and the gallbladder may be required. Blood studies, as well as agglutination tests, may be necessary for the diagnosis. Except in the very acute diarrheas, an entiologic diagnosis is required before treatment can be planned.

Acute diarrheas may be classified: simple, infectious, toxic, allergic, or a manifestation of acute febrile disease. Chronic diarrheas are grouped under infectious, deficiency states, allergic (emotional, and those caused by organic lesions involving the ileum, colon, and rectum. If the entiologic factor is established, then we have specific therapy for most of the infectious diarrheas. Symptomatic treatment should not be prolonged as it increases the morbidity and may give time for irreversible changes to occur or malignancy to advance to an inoperable stage.

For the chronic diarrheas, a more thorough study of the patient is essential. Deficiency states may be the cause or result of diarrhea. Regional ileitis and chronic nonspecific ulcerative colitis may have more than one cause, for example: emotional tension, allergies, endocrine dysfunction, and previous trauma from coarse food, drugs, and secondary bacterial invasion. The treatment here must be directed to all factors. Diverticulosis of the colon is a common disease in older people. Diverticulitis is frequently associated. If bleeding occurs, malignant changes must be sought. One cannot overstress the importance of an early diagnosis of tumors because it is only then that surgery offers good results. 8 references.—*Author's abstract.*

BLOOD AND LYMPHATIC DISORDERS AND DISEASES

The Effect of a Diet of Vegetable Foods on the Blood Picture. OLA K. GANT AND ERNEST CHRISTENSEN, Loma Linda, Calif. Department of Therapeutics, College of Medical Evangelists. Int. Rec. Med. *164*:79-86, Feb. 1951.

Twenty "normal" subjects were maintained on a diet of fruits, grains, nuts, and vegetables for a period of twelve weeks. Five of these subjects remained on the diet for a full year. A certain range of food selection was permitted, but each subject recorded his food intake. Comparisons were made with the recommended allowances of the National Research Council. Calcium and riboflavin were the only factors of those calculated that were significantly low in the diets chosen. Blood analyses revealed no change in number of red cells, hemoglobin level, or total serum protein, but the blood cholesterol decreased in the majority of cases. There was a slight initial loss of weight in some cases. The diet was subjectively reported as satisfactory.

Haemopoietic Activity of Vitamins B_{12c} and B_{12a} in Pernicious Anaemia. J. N. MARSHALL CHALMERS, *London*, England. Brit. M. J. *No. 4699*:161-64, Jan. 27, 1951.

Crystalline vitamin B_{12c} and vitamin B_{12a} derived from *Streptomyces griseus* were isolated by Lester Smith (1950). These factors differ from vitamin B_{12} itself and from vitamin B_{12b}. They are chromatographically distinct and have different properties on microbiologic assay. Nine cases of pernicious anemia in relapse have been treated with crystalline vitamin B_{12c} and 5 cases with crystalline vitamin B_{12a}. Hemopoietic activity of both these factors was demonstrated following intramuscular injection of 20 mcg. material in each case. The primary responses show that the clinical activity of these factors is of about the same order as could be expected from an equivalent amount of crystalline vitamin B_{12} itself. Follow-up studies are being made. 14 references. 2 tables. 1 chart.—*Author's abstract.*

Effect of Vitamin B_{12c} in Pernicious Anaemia and Subacute Combined Degeneration of the Cord. C. C. UNGLEY AND H. CAMPBELL, Newcastle-upon-Type, England. Brit. M. J. *No. 4699*:152-57, Jan. 27, 1951.

The efficacy of vitamin B_{12c} in pernicious anemia was assessed and compared with that of vitamin B_{12}. Single doses given intramuscularly were graded logarithmically from 10 to 160 μg. Twenty-eight responses were observed in 24 patients.

Reticulocyte responses were assessed, but conclusions were based on the increase of red blood cells in 15 days. This was compared with the expected response according to a formula suggested in the authors' previous work (Brit. M. J. *2*, 1370, 1949). There were the usual individual variations, but the mean of the 28 responses was almost identical to that expected from similar doses of vitamin B_{12}, and the logarithmic dose-response curve did not differ significantly from that of vitamin B_{12}. Doses of 40 μg. and over gave more consistent responses than smaller doses.

It is pointed out that a difference of 30 per cent in hematopoietic potency between vitamins B_{12} and B_{12c} would result in only a difference of about 5 per cent in the average response of 28 cases; but belief in their smiliarity was strengthened by later analyses based on increases in 15 days of hemoglobin and packed cell volume.

The usual improvement in well-being, gain in weight, relief of sore tongue, and gastro-intestinal symptoms, was noted. The leukocyte level usually returned to normal.

Direct evidence of the efficacy of vitamin B_{12c} against the neurologic manifestations of pernicious anemia was obtained by treating 6 established cases of subacute combined degeneration, 2 of whom were subject to quantitative studies. There were also 8 patients with minor neurologic involvement. Of the 14 cases none became worse and 12 improved.

Excluding cases with neurologic involvement, 20 patients were maintained for periods of four to nine months on a dose of 10 μg. every two weeks. This proved adequate, and none of the patients showed any symptoms of relapse; temporary, slightly subnormal, red blood cell or hemoglobin levels were rectified by the administration of iron in one patient and in another normality was restored without change

of treatment. One patient had a slightly raised M.C.V. during the maintenance period.

Such low doses are justifiable only on experimental grounds and where the patient is kept under close supervision. The suggested routine dosage for uncomplicated cases is at least 60 μg. every three weeks, and more if there is neurologic involvement or intercurrent infection. 4 references. 5 figures. 3 tables.—*Author's abstract.*

Vitamin B_{12} and Folic Acid in Megaloblastic Anaemia after Total Gastrectomy. NANCY S. CONWAY AND HUGH CONWAY, Glasgow, Scotland. Brit. M. J. *No. 4699*:158-61, Jan. 27, 1951.

A case of megaloblastic anemia following total gastrectomy performed for the effects of corrosive poisoning is described. The anemia was first diagnosed six years after the operation. Vitamin B_{12} produced striking clinical improvement, but the reticulocyte response and the rise of red blood cells in the first 15 days were less than expected in Addisonian pernicious anemia of equivalent severity. Vitamin B_{12} failed to raise the red cell count above 3.80 ml. per cu.mm., but the addition of folic acid brought about complete hematologic remission. Various aspects of the pathogenesis of postgastrectomy macrocytic anemia are discussed. It is claimed that this is the first case of megaloblastic anemia following total gastrectomy to be treated with vitamin B_{12}, and the therapeutic result is considered to support certain experimental work which suggests that both vitamin B_{12} and folic acid are essential for the maturation of erythrocytes. 34 references. 2 tables.—*Author's abstract.*

The Effect of Aureomycin upon Hodgkin's Disease. RALPH GOLDMAN, Los Angeles, Calif. Am. J. M. Sc. *221*:195-98, Feb. 1951.

Five patients with Hodgkin's disease in varying stages, but all with fever, were given standard doses of aureomycin without any apparent alteration in their clinical course. Four patients subsequently were given nitrogen mustard, and 3 of these responded with a prompt, complete, but temporary remission. This suggests that organisms susceptible to aureomycin play no part in the etiology of Hodgkin's disease. 5 references. 1 figure.—*Author's abstract.*

The Effect of Orally Administered Desiccated Beef Spleen and Abdominal Lymph Nodes on Megakaryocytogenesis and Thrombocytes. E. M. SCHLEICHER, Minneapolis, Minn. Acta haemat. 5:143-50, March 1951.

Desiccated normal beef spleen and abdominal lymph nodes were given orally to normal individuals and to patients with diseases affecting megakaryocytogenesis and the number of thrombocytes in the peripheral circulation. The desiccated material contained a substance which directly or indirectly affected megakaryocytogenesis and number of thrombocytes, with maximal response of the latter between the third and fifth day. The reaction was transitory, uniform and reproducible.

In normal individuals no appreciable acceleration of megakaryocytogenesis occurred but an increase of the number of thrombocytes in the peripheral circulation could be demonstrated.

In patients with Addison-Biermer's (pernicious) anemia in relapse the megakaryocytogenesis became accelerated and a definite rise of the number of thrombocytes occurred. In full remission, however, the increase of thrombocytes was not accompanied by a production of megakaryocytes above the normal maximal figures.

A decrease of the number of peripheral thrombocytes was observed in the patients with essential thrombocytopenic purpura, but a distinct increase of immature megakaryocytes could be demonstrated. While the thrombocytes decreased in the patient with myeloid leukemia, no significant alterations occurred in the megakaryocytogenesis.

It is suggested that a decrease of the peripheral thrombocytes on the described test may be an aid in detecting splenic dysfunction.

The Value of Red Cell Survival Studies. BEN FISHER, Chicago, Ill. Am. Pract. 2:29-31, Jan., 1951.

It is often difficult to differentiate between congenital and acquired spherocytic hemolytic anemias. This is especially true in adults and in young children, when other siblings are not available for study. Examination of the bone marrow may give no clue except in the "symptomatic" hemolytic anemias associated with lymphomas or metastatic carcinomas. This differentiation is important in offering a prognosis as to the remission following splenectomy.

Using the Ashby technic, the erythrocytes of fresh blood will be found to have a normal life survival (120 days) when transfused into a patient with congenital spherocytosis. When transfused into a patient with an immunologic type of acquired hemolytic anemia, the survival time will be greatly shortened. The resulting plotted curve will assume an exponential form instead of the normal straight line of decay.

A case is presented which illustrates the use of the Ashby technic in a patient with an acquired hemolytic anemia. 9 references. 1 figure.—*Author's abstract.*

Six Blood-Group Antibodies in the Serum of a Transfused Patient. R. K. WALLER, Virginia, and R. R. RACE, London, England. Brit. M. J. *4700*:225-26, Feb. 3, 1951.

The purpose of this note is to call attention to another instance of formation of multiple blood-group antibodies after transfusion. The recipient, a 30 year old negro suffering from an undiagnosed collagic disease, received three transfusions for a severe hypochromic anemia. Five days later he was severely jaundiced, and his urine was blood-stained. Six weeks later it became advisable to transfuse the patient again, but at this time it seemd impossible to crossmatch him successfully. His red cells belonged to the B N S- Rh_o Fy^a- group. By means of multiple testing and absorption procedures, it was demonstrated that the patient's serum contained anti-A, anti-M, anti-S, anti-C, anti-E, and anti-Duffy. After exclusion of these factors from the donor cells, the patient was transfused successfully many times. Attention is called to the possible relationship between the unusual ability to produce blood group antibodies and collagic disease. 2 references. 2 tables.—*Author's abstract.*

The Nervous-Humoral Regulation of the Leukocytes. G. ROSENOW, New York, N. Y. Acta Haemat. *5*:1-18, Jan., 1951.

Mechanical or electrical stimulation of the hypothalamic region is followed by a rapid onset of a marked neutrophilic leukocytosis with shift to the left. This leukocytosis indicates an increased reactivity of the bone marrow.

The respective areas can be incapacitated temporarily by luminal, which acts mainly on the brain stem. Luminal inhibits leukocytosis by bacterial protein but does not inhibit abacterial leukocytosis. This seems to indicate that the mechanism of abacterial and bacterial leukocytosis is different.

Narcotics such as chloral hydrate, which act predominantly on the cortical regions of the brain do not inhibit the induction of leukocytosis. Antipyrin, in spite of its marked effect on the body temperature, is without inhibitory influence on the induction of leukocytosis.

The data reported in detail further support the concept of a regulating role of the diencephalon (especially the hypothalamic area) for reactive leukocytosis.

These regulations, though cerebrally initiated and governed, are of a humoral nature, as shown by experiments on parabiotic animals and by experiments about the mechanisms of ACTH.

Nervous stimuli seem to liberate in the liver effector substances which in turn act on the bone marrow.

The Sedimentation Reaction in Relation to the Plasma Protein as a Criterion of Therapeutic Effect. A. WESTERGREN AND S. STAVENOW, Stockholm, Sweden. Acta Med. Scandinav. *139*:214-28, f. 1, 1951.

The results are presented of complete plasma protein analyses in 37 tuberculotics before and after chemotherapy (PAS, Streptomycin, and Diason). During treatment the fibrinogen and serum globulin decreased (and the albumin rose) in pronounced correlation with the sedimentation rate. (General correlation coefficient 0.87.) Of the electrophoretic serum globulin fractions, the α fraction showed a marked decrease, the β fraction an inappreciable decrease, and the γ fraction remained, on the average, unchanged. As regards the relation to the sedimentation reaction a certain discrepancy was observed: the α fraction showed a marked correlation before treatment but not after, but the γ fraction a slight average relation only in the treated cases. The cholesterol presented no change nor relation to the sedimentation rate.

A detailed discussion follows regarding the significance of the reduced sedimentation, with special reference to the hypothesis of "liver damage", the writers adducing clinical examples and comparing the temperature and white blood picture, etc. There seems no reason on the whole to reckon with a different pathophysiologic basis for the reduced sedimentation rate following chemotherapy in tuberculosis (nor, probably, in other circumstances) than for the same phenomenon following a "natural" improvement. The writers caution against drawing conclusions as to serologic and immunologic conditions on the basis of the nonspecific changes in the plasma protein picture.

Certain experiences and hypotheses reported with regard to the sedimentation rate and blood proteins in connection with Conteben treatment appear to be misleading.

In conclusion the writers discuss the influence of the red blood cells on the sedimentation rate, among other things, with reference to the carbon dioxide content of the blood, and offer a few remarks on the sedimentation test technic and the "normal" limits of the sedimentation reaction.

Femoral Venous Blood Oxygen Studies upon Normal and Abnormal Subjects at Rest and after Exercise. V. H. WILSON, Johannesburg, South Africa. South African J. M. Sc. *15*:115-19, Dec., 1950.

The femoral venous and the arterial blood oxygen at rest and after exercising the legs have been studied in 4 normal subjects, in 4 patients with anemia, in 6 patients with respiratory disease without anoxemia, and 7 anoxemic patients with respiratory disease.

In most of the normal and abnormal subjects a striking fall of the femoral venous blood oxygen percentage saturation following exercise of the legs has been demonstrated.

In 2 anemic patients and 1 with anoxemia, estimation of the femoral venous blood oxygen unsaturation suggested that all the oxygen had been dissociated from the hemoglobin after exercise.

A Practical Method of Intra-Arterial Transfusion. K. M. LIPPERT, I. K. FURMAN, Columbia, S. C. J. South Carolina M. A. *47*:63-65, Feb., 1951.

Intra-arterial transfusion should be employed only in severe emergencies in selected cases. Although profound shock which does not respond to any medical treatment is always a positive indication, the procedure is effective most dramatically in cases of good cardiac reserve which have experienced acute blood loss. A practical method of application is briefly as follows: The radial artery is located, and by an incision directly over it, a large bore needle (#12) or, by preference, a canula, is inserted into the artery, directed toward the heart, and temporarily fastened by a silk ligature proximal to a small incision through the arterial wall. A regular transfusion set is connected to this needle or canula and a series of transfusion bottles are joined so that the blood passes from the first bottle into the artery under pressure while blood from the second or third bottle is forced forward into the first bottle. In order to obviate any accidents by forcing air into the system and also to prevent a backflow of blood into the air pressure system, a bottle containing only 40 cc. of citrate solution is inserted at the end of the series. Air pressure is applied through a large needle inserted into the center glass tube of the bottle containing the citrate solution. This needle is connected to a rubber tubing arranged in a "Y" formation with a regular blood pressure bulb on one arm of the "Y" and a blood pressure manometer on the other arm of the "Y." In operation, the bulb is pumped until the manometer registers the desired blood pressure, which in cases

of extreme shock should not be too rapidly raised, and a clamp then applied across the tubing just beyond the bulb to prevent any leakage of air pressure. The air passes into the bottle containing citrate and exerts pressure by means of the connecting tube, which extends above the level of the citrate in the bottle, against the blood in the intermediate transfusion bottle, forcing this blood into the first transfusion bottle and hence into the patient's artery. By this technic it has been possible to return a patient from profound shock, the result of blood loss, to a blood pressure state approximately normal within a very few minutes, and by containing the flow of blood, using as much as 4,000 cc. maintaining a normal blood level cntinuously for three to four hours. In severe emergency, glucose solution and plasma have been similarly employed for shorter periods of time until blood became available.

Certain complications sometimes arise due to accidental obliteration of the radial artery in instances where there is poor collateral circulation in the hand. This has been known to have caused a mild degree of ischemic necrosis. There are also instances of apparent acute arterial spasm which may be the result of cold solutions entering the artery, causing reflex vasomotor disturbance, or possibly the result of injection of hypo-oxygenated blood into the local circulation for a considerable period of time. 3 references. 1 figure.—*Author's abstract.*

The Effect of Para-Aminobenzoic Acid (PABA) or Its Sodium Salt on the Erythrocyte Sedimentation Rate in Vitro. J. C. HAYWARD and G. T. HARRELL, Winston-Salem, N. C. North Carolina M. J. *12*:47-49, Feb., 1951.

Blood was studied from 14 hospitalized patients with no history of rheumatic disease or of therapy with salicylates or para-aminobenzoic acid. Sedimentation rates were done on the blood after addition of PABA so that the final concentration ranged from 10 to 70 mg. per 100 cc. Duplicate tests on 4 patients were done using PABA and its sodium salt.

Neither para-aminobenzoic acid (PABA) or its sodium salt in concentrations as high as 50 mg. per 100 cc. significantly altered the sedimentation rate of blood in vitro. Concentrations in the blood above this level are rarely encountered in patients receiving PABA therapeutically. The slowing of the sedimentation rate observed at 60 to 70 mg. per 100 cc. was felt to be of no clinical significance. 5 references. 1 figure. 2 tables.—*Author's abstract.*

ALLERGIC DISORDERS AND DISEASES

Sudden Death from Asthma. CHARLES H. A. WALTON, D. W. PENNER, and J. C. WILT, Winnipeg, Canada. Canad. M. A. J. *64*:95-102, Feb., 1951.

Previous pathologic reports of death from asthma are briefly reviewed. While the pahtologic characteristics have been widely published, the authors feel that it is insufficiently appreciated that patients can die from asthma itself. The uniformity of findings in published cases is stressed.

Thirteen cases are reported with brief clinical summaries and pathologic findings. Age at death ranged from 14 months to 61 years. Death occurred in an asthmatic attack in 12 cases and in 1 the patient died of congestive heart failure from Cor pulmonale. Heavy sedation preceeded death in 9 cases, and the dangers of morphine, demerol, intravenous anesthetics, and curare are stressed.

Five pathologic features were found consistently in all cases, i.e., voluminous lungs, mucus plugging, emphysema, and eosinophilic infiltration of the bronchial walls. Right heart hypertrophy was present in 6 cases but in only 1 was Cor pulmonale evident clinically. Hypertrophy of the bronchial walls was not prominent in these cases. Epithelial hyperplasia was striking in 3 cases. Mucus glands were increased in only 1 case, but goblet cells in 7 were increased.

It is emphasized that the autopsy findings in cases dying from asthma are characteristic and that a diagnosis of death from bronchial asthma can be made at autopsy in the absence of a clinical history. Death appears to be due to asphyxia from widespread bronchial plugging. 5 references. 7 figures.—*Author's abstract.*

Allergic Granuloma of the Lung. Clinical and Anatomic Findings in a Patient with Bronchial Asthma and Eosinophilia. JOSEPH C. EHRLICH, AND ALFRED ROMANOFF, New York, N. Y. Arch. Int. Med. *87*:259-68, Feb. 1951.

A case of allergic granulomata of the lungs in a 49 year old man with asthma and eosinophilia, who died from asphyxia ten days after the onset of his illness, is reported.

The autopsy findings revealed in the lungs two tumor-like masses which grossly were firm, yellow in color, and showed a large central area of necrosis. Microscopically these masses disclosed an exudative pneumonitis with necrosis and numerous vascular lesions. Giant cells, edema, and fibrinoid swelling of collagen were also seen. An unusual lesion due to interfibrillar edema, collagen fiber swelling, and infiltration by eosinophiles, plasma cells, and foam cells, led to a bulbous swelling of the alveolar wall. This parenchymal pulmonary lesion was found in the region of the infilterate and not elsewhere, therefore suggesting an allergic basis. Eosinophilic infiltrations were also found in the epicardium, diaphragm, intestinal wall, hilar lymph nodes, and stomach. In view of the asthma, eosinophilia, and pulmonary findings, it is likely that a diagnosis of Loeffler's syndrome would have been made clinically if the patient had been x-rayed and observed long enough.

Lesions in other organs besides those found in the lungs in our case and in other cases reported indicate that Loeffler's syndrome is an essentially systemic disease and that the concept has been too narrowly focused on the pulmonary manifestations.

In addition to the transitory pulmonary lesions described clinically and by x-ray in Loeffler's syndrome, the postmortem findings in this case and in others reveal that some of the pulmonary lesions may be of relatively long duration. Furthermore, it should be borne in mind that more severe forms of allergic diseases may develop with involvement of extrapulmonary organs and the general vascular system, and some of these cases may terminate fatally, usually with the anatomic findings of periarteritis nodosa and allergic granulomatosis. 9 references. 9 figures.—*Author's abstract.*

DEFICIENCY DISEASES AND METABOLIC DISORDERS

Protein Feeding and Blood Sugar Levels in Diabetes. ERIC R. GUBBAY, Winnipeg, Canada. Canad. M.A.J. *64*:150-52, Feb. 1951.

The question, "Will protein feeding cause hyperglycemia in treated patients who are adequately controlled, or will such feeding prevent insulin hypoglycemia?", has been studied and some relevant facts reported.

Two patients showed the occurrence of spontaneous falls in blood sugar levels after protein feeding, maximum fall 30 mg. per cent. Four patients showed rise in the blood sugar after protein feeding, maximum rise 40 mg. per cent. Protamine zinc insulin hypoglycemia was not reversed after feeding protein in 1 patient only. Toronto insulin hypoglycemia was not prevented by protein feeding in 2 patients. Such hypoglycemia was appreciably less after protein in the third patient so studied. Reference is made to the work of Conn and Newburgh whose findings are in accord with the results reported in this study. It is concluded that the slow conversion of protein to glucose causes small, and often unimportant, effect on the blood sugar of well controlled diabetic patients, either in promoting hyperglycemia or in preventing hypoglycemia. 3 references. 1 table.—*Author's abstract.*

Diabetic Retinopathy. L. BENJAMIN SHEPPARD, Richmond, Va. Quart. Rev. Ophpth. *7*:1-31, March 1951.

This paper reviews the literature pertaining to diabetic retinopathy and the related fundamentals of this metabolic disease. The ophthalmologist has the responsibility for the interpretation of this metabolic disturbance, in order that the eye findings may be correlated with the data of the diagnostician in such a way that the patient may receive the maximum benefit.

Diabetes affects the eye in many ways. The findings of persistent punctate retinal hemorrhages in a fundus that is otherwise normal strongly suggest that the lesion is diabetic. Punctate exudates and other changes in the terminal vascular bed may follow. The importance of early and regular ophthalmoscopic examinations cannot be overstressed. The duration of the disease is important, but constant individual control is the most important single safeguard against diabetic ocular complications. Uncontrolled diabetes permits wide daily fluctuations in the blood sugar, with deviations from normal physiology, thereby prematurely producing nutritive and secondary tissue changes.

We have not yet accumulated sufficient data to answer completely the questions how and why these vascular changes occur in diabetes mellitus, but the retinal pathologic findings involve numerous factors in addition to hyperglycemia. The metabolic instability in the diabetic state may be a potent factor in producing the abnormal changes in the vascular and nervous systems.

The studies of many older diabetics show that there is more than a coincidental relationship between the degenerative vascular changes in the eye and those in the kidney. In addition to a discussion of the eye findings, the following related topics are

presented: (1) etiology, with special references to the endocrine system; (2) pathogenesis, with discussion of the concepts, metabolic disturbance, hormonal relationship, relation of the kidney and the liver, vascular changes, with particular reference to the terminal vascular bed, and biochemical changes; (3) treatment, a discussion of the topics of control, diets, and insulins; and (4) suggestions for clinical and experimental studies.

The solution of the problems besetting the diabetic state may be found by coordinated study, with the close collaboration of the pharmacologist, the biochemist, the pathologist, the ophthalmologist, and the physiologist. 151 references. 7 (color) figures. —*Author's abstract.*

Constitution and Insulin Sensitivity in Diabetes Mellitus. JOHN LISTER, JOHN NASH, AND UNA LEDINGHAM, The Royal Free Hospital, London, England. Brit. M. J. *1*:376, Feb. 24, 1951.

In this paper an attempt has been made to correlate constitutional types with insulin sensitivity in diabetic patients. Several clinical types of diabetes mellitus have long been recognized and, in particular, the young thin patients with an acute onset and the older obese patients with a gradual onset of the disease are two well recognized types. Himsworth (1936), using his insulin sensitivity test, found that, in general, the first group of patients showed a sensitive response to the test whereas those in the second group tended to be insensitive. He thought that possibly the diabetic state resulted in the first group from an insulin deficiency whereas in the second group there is rather an insensitivity to the action of insulin.

The present writers claim that the most important determining factor in insulin sensitivity is probably the constitutional make-up of the patient and that there is a group of patients of characteristic physique who are almost uniformly insensitive in their response to insulin. In these cases the features are small and the bones are generally slender with tapering extremities, the skin is fine and the hair is silky, the teeth are often large and well spaced and the nails are well shaped and of good texture. Obesity is a frequent finding and usually of girdle distribution, but it is not an essential of the type. The authors further claim that they can divide the patients in their clinic into those with an unremarkable constitution (Type I) and those showing the characteristics outlined above (Type II).

Insulin sensitivity tests were carried out on 100 unselected patients attending the clinic at the Royal Free Hospital. The sensitivity was found to range from zero to just above 2, the mean for the whole series being 0.65. In dividing the patients into the two clinical types it was found that 38 of the patients were Type I, 37 were Type II, 27 were unclassified and 5 were discarded owing to incomplete data. The mean insulin sensitivity of the Type I cases was 0.78, which was well above the average of 0.65 for the whole series, while the mean sensitivity of the Type II patients was well below that mean, being 0.48.

The authors compared their findings with a constitutional study carried out by Draper, Dupertuis, and Caughey (1944) who somato-typed a series of diabetics and observed that two clearly different morphologic types could be recognized, the first

being of linear form and the second being of more rounded form. Furthermore, these workers found that the patients in the first group were clinically sensitive to insulin and became ketosed with poor control, while the patients of the second group were, in general, less sensitive to insulin and had little tendency to ketosis or hypoglycemia.

In conclusion, the present authors claim that there are two clinical types of diabetics which can be identified by their appearance; the first type (Type I) being of unremarkable constitution, and the second type (Type II) having characteristic features. The mean insulin sensitivity of the Type I patients was significantly higher than that of the Type II patients.—*Author's abstract.*

Obesity in Diabetes: A Study of Therapy with Anorexigenic Drugs. KERMIT E. OSSERMAN, AND HENRY DOLGER, New York, N. Y. Ann. Int. Med. *34*:72-79, Jan. 1951.

Because of the inability to maintain adequate dietary control in a large group of obese diabetic patients, the limited facilities for psychotherapy, and the impracticability of its widespread application, an investigation was undertaken to study the effects of the anorexigenic drugs upon these individuals.

Fifty-five obese diabetic patients attending the diabetic clinic of the Mount Sinai Hospital were selected for investigation. Thirty-one of the patients were being treated with insulin. Essential hypertension was present in 30 patients. During the period of investigation, which lasted from 18 to 30 months, each patient was examined fortnightly. During the first 18 months of investigation, patients not receiving insulin were subjected monthly to glucose tolerance tests.

Following the initial examination, a diet of 1,000 calories was prescribed. Anorexigenic drug therapy, in the form of dl-amphetamine sulfate, "benzedrine", was prescribed in doses of 5 mg. before breakfast and luncheon. This was inadequate in most instances, and the dose was increased to 30 mg. daily (10 mg. before breakfast, before luncheon, and at 4 p.m.). After three months, 3 of the hypertensive patients showed further elevation of blood pressure, and d-amphetamine sulfate, "dexedrine", was prescribed in the same dosage, with the return of blood pressure to premedication levels. Thereafter, 48 of the 55 patients were treated with d-amphetamine sulfate. It was our experience, in this study, that equivalent anorexic effects were obtained with the same dose of either isomer.

For the past year, anorexigenic drug therapy was discontinued on all but 5 patients. The remaining 50 patients were continued, under observation, on low caloric diets. Eleven of these did not return at regular intervals and, therefore, were dropped from the latter part of the investigation.

Thirty-six of 55 obese diabetic patients exhibited significant loss of weight (11 to 77 pounds) on low caloric diets aided by anorexigenic drug therapy.

The most successful results were obtained in the 31 patients receiving insulin before the investigation. Fifteen patients were able to discontinue insulin administration. Fairly rapid reduction of insulin dosage was often necessary to avoid hypoglycemic reactions following marked decrease in food intake. Dl-amphetamine sulfate, or its isomer, did not obscure the hypoglycemic symptoms. Eleven patients obtained reduction in dosage after significant loss of weight, as much as 70 units per day.

In the milder group of diabetics, 32 per cent had improvement of tolerance as shown by monthly glucose tolerance tests.

One year after anorexigenic drug therapy had been withdrawn, 19 per cent exhibited further, but minor loss of weight, and 41 per cent regained less than 10 pounds, whereas 40 per cent of the group regained appreciable weight, from 11 to 26 pounds.

Follow-up one year after withdrawal of anorexigenic drug therapy revealed that one third of the patients did retain their loss of weight.

Of the 31 patients who originally required insulin, 23 have been followed for the past year; 50 per cent resumed insulin administration upon weight gain.

A few of the patients showed reactions such as nervousness, palpitation, or insomnia. Generalized dermatitis occurred in two instances. An undesirable effect on blood pressure was observed in only 4 patients. No serious complications were noted; the anginal syndrome was not provoked, nor did any instance of coronary occlusion occur. Despite the absence of serious complications in this group, anorexigenic drugs should be used cautiously in patients with significant myocardial damage.

Weight reduction in obese diabetic patients has been notoriously difficult to achieve; most need some supportive treatment. For this special type of patient, anorexigenic drugs proved valuable for short-term therapy. However, when the drug was withdrawn, the majority of patients again displayed laxity in adhering to diet control.

Obese diabetic patients have an added incentive towards weight reduction in the expectation that they may be able to discontinue insulin administration.

Caloric restriction should remain the basis of the treatment of obesity in diabetes mellitus. Anorexigenic drugs played no direct role in the improvement of carbohydrate tolerance. They simply helped 65 per cent of the group to display better cooperation in dieting and permitted them to achieve striking reductions, even cessation of insulin therapy. Once anorexigenic drug treatment was withdrawn, only one third of the patients continued to maintain their lower levels of weight. In this study, we found no contraindications to the use of anorexigenic drugs for the selected obese individual with diabetes mellitus. 18 references, 6 tables.—*Author's abstract.*

The Newer Insulins and Some of the Complications of Insulin Administration. H. B. MULHOLLAND, Charlottesville, Va., West Virginia M. J. *47*:53-57, Feb. 1951.

This paper presents in some detail the approach to the modern diabetic patient, insofar as diet and treatment with insulin is concerned. It is pointed out that with the use of a relatively normal type of diet, including such foods as bread, potatoes, rice, and grits, and the understanding of the uses of insulin and its newer modifications, good control can be obtained. A history of the modification of insulin is presented, showing how an attempt has been made to prolong the action on the blood sugar by use of protamine, globin, and various substances. Charts are shown demonstrating the time-action curve of the various insulins including regular insulin, protamine zinc insulin, globin zinc insulin, 2:1 mixtures, NP-50 and NPH-50.

Our experience using the various types of long-acting insulin on 21 selected diabetics, most of whom are quite severe, is shown graphically. Of the four types, we found that in these cases NPH and globin proved most satisfactory, NPH slightly more than

globin. The 2:1 mixture was much better than protamine zinc insulin alone. The question of individualizing in the treatment of diabetes, particularly in severe cases, was emphasized. Furthermore, the management of brittle diabetes was discussed, and the cause of insulin resistance and atrophy were gone into at some length. 10 references. 9 charts.—*Author's abstract.*

Raised Blood Pyruvic Acid Level in Diabetic Acidosis. The Value of Cocarboxylase in Treatment. I. C. GILLILAND, AND M. M. MARTIN, London, England. Brit. Med. J. *4696*:14-16, Jan. 6, 1951.

Prolonged severe diabetic ketosis is associated with a metabolic disturbance of carbohydrate oxidation, as suggested by the recent finding of a raised pyruvic acid level in the blood in diabetic precoma or coma. Oxidation of pyruvic acid is effected by pyruvic oxidase, which is active only in the presence of the coenzyme cocarboxylase. Accumulation of pyruvic acid in the blood suggests a failure of this enzyme system.

Twelve alloxan diabetic rabbits were selected in pairs as having reached approximately the same stage of precoma at about the same time after alloxan administration. Each pair received identical general treatment with fluids and insulin. In addition, one of each pair was given two hourly 25 mg. cocarboxylase intravenously and 10 mg. riboflavine subcutaneously. Four acidotic diabetic patients were also treated in a similar fashion in pairs, one of each pair receiving cocarboxylase and riboflavine in addition to the standard treatment. Neither in the rabbits nor in the human beings was any difference observed between the cocarboxylase treated ones and the controls, either in the rate of clinical recovery, lowering of the raised level of the blood pyruvic acid and the blood sugar, or in the return to normal of the alkali reserve.

Markees and Meyer (1949) and Boulin et al (1949) reported that the administration of cocarboxylase to the standard treatment of diabetic coma lowered the raised blood pyruvic acid level and hastened recovery. Thus, while the authors confirmed the evidence of defective pyruvic acid oxidation in diabetic acidosis, they found no evidence that this was due to a deficiency of cocarboxylase. They suggested that the cause of the raised level of the pyruvic acid in the blood may be therefore due to an inhibition or partial inactivation of the protein component of the enzyme system. 14 references. 2 figures.—*Author's abstract.*

Cortisone as an Adjunct in the Therapy of Acute Gout. R. D. FRIEDLANDER, San Francisco, Calif. J.A.M.A. *145*:11-14. January 6, 1951.

A case of acute interval gout is reported in which the relief following the administration of cortisone was both rapid and dramatic. Cortisone was not administered in this case until the usual methods of treatment had failed. This case is reported as confirmatory evidence of similar instances in which it has been demonstrated that the use of pituitary adrenocorticotropic hormone (ACTH) and colchicine has proved valuable in the termination of an acute attack of interval gout. It is suggested that cortisone is a more efficacious therapeutic agent in such cases than pituitary adrenocorticotropic hormone and that it may prove in the future to be an important means of preventing tophaceous gout. 11 references.—*Author's abstract.*

Cortone Therapy in Acute Gout. NATHAN BLOOM, Richmond, Va., Virginia M. Monthly. *78*:84-86, Feb. 1951.

Acute gout is now considered a hypersensitive reaction. It has been suggested by Harkavy that an individual suffering with gout may be regarded as a potentially allergic patient whose joints constitute the major shock tissue with a coincidental uric acid diathesis. This is a case report on a patient with acute gout treated with large doses of cortone over a period of 18 days. There was definite improvement within 48 hours by treatment. This improvement was maintained for some time, but a remission occurred due to the patient's returning to work too soon. There were no changes in the laboratory studies during the treatment. The most remarkable effect of cortone was on the toxic manifestations, such as irritability and lethargy, which always accompany severe gout. It is suggested that this drug and ACTH be used at the onset of an acute attack, probably in smaller doses and for a period of 24 hours, combining the hormone treatment with colchicine. 2 references.—*Author's abstract.*

Combined Administration of Desoxycorticosterone Acetate and Ascorbic Acid. I. Clinical Results in Rheumatoid Arthritis and Laboratory Studies. J. B. R. MCKENDRY, C. A. SCHAFFENBURG, AND E. PERRY MCCULLAGH, Cleveland, Ohio. Arch. Int. Med. *87*:190-8, Feb. 1951.

On the basis of European reports of antirheumatic activity from combined administration of desoxycortisterone acetate (DCA) and ascorbic acid, clinical trials of the method were carried out in 23 cases of rheumatoid arthritis. The suggested daily dosage of 5 mg. of DCA in oil intramuscularly, followed in a few minutes by 1000 mg. of ascorbic acid in aqueous solution intravenously, was employed.

Sixteen of the 23 patients received more than two such treatments, and of these, 9 showed definite subjective or objective improvement within a few days. Case reports on the improved group were analyzed in an attempt to determine the reason for the observed changes. In most of this group it was the impression that the beneficial results could be attributed to the effects of suggestion or concurrent physiotherapy. However, there remained a few cases in which it was difficult to deny the probability of some therapeutic activity of one or both of the substances administered.

Combined therapy with DCA and ascorbic acid did not appear to exert any cortisone-like activity as judged by failure to influence the number of circulating eosinophils, the dextrose tolerance, or the urinary excretion of nitrogen, electrolytes, 17-ketosteroids, or corticoids in normal volunteers or in the rheumatoid arthritis patients. 8 references. 2 tables.—*Author's abstract.*

Recent Advances in Therapy with ACTH and Cortisone. L. I. GARDNER, Baltimore, Md. North Carolina M. J. *12*:41-46, Feb. 1951.

Rational use of ACTH, cortisone, or compound F depends upon a clear understanding of the physiologic action of these agents; hence their similarities and differences have been reviewed. Of particular importance is the opposing action of ACTH and cortisone on adrenal activity; the former causes hyperfunction and the latter atrophy.

Evidence is presented supporting the hypothesis that administered cortisone suppresses endogenous ACTH production.

A progress report is made on therapeutic results obtained in the past year with ACTH and cortisone, emphasizing the latter. Wilkins et al and Bartter et al have made almost simultaneously the gratifying discovery that cortisone produces normal feminization of female pseudohermaphrodites. As a result, a bright therapeutic outlook can be offered these patients. Results are also presented on ACTH-cortisone treatment of rheumatoid arthritis, acute rheumatic heart disease, gout, hypersensitivity syndromes, burns, and surgical cases.

A number of disappointing clinical results are listed. Undesirable side effects are described, such as the development of Cushing's syndrome medicamentosa (hirsutism, acne, hypokalemia, and hypochloremic alkalosis). The tapering off of medication to lessen post-treatment hypoadrenocorticism is described. 26 references. 2 figures. 3 tables.—*Author's abstract.*

Rheumatoid Arthritis. CHARLES RAGAN, New York, N. Y. Bull. New York Acad. Med. *27*:63-74, Feb. 1951.

The accepted forms of therapy in rheumatoid arthritis have been evaluated in relation to the natural history of the disease when studied over a five year follow-up period. In the experience of the author, no form of therapy advocated in the precortisone era has modified the disease whereby 50 per cent do fairly well and 50 per cent do badly. Of the 50 per cent with the bad prognosis, one-third do poorly and end as cripples. The use of cortisone or ACTH in conjunction with measures of physical medicine and orthopedic surgery has been encouraging in the short period of observation and may hold out hope to that group of patients who formerly did badly. 11 references. 3 figures. 2 tables.—*Author's abstract.*

The Place of Cortisone in the Treatment of Chronic Progressive Polyarthritis (La place de la Cortisone dans le traitement de la polyarthrite chronique progressive). J. MICHEZ, E. COLINET, AND P. E. ORTEGAT, Hopital Universitaire Saint-Parre, Brussels, Belgium. Bruxelles-méd. *31*:403-17, Feb. 25, 1951.

Eight cases of progressive polyarthritis are reported in which cortisone was used in treatment. All of these patients showed some degree of improvement, which was limited to relief of pain in 1 case in which the patient had been bedridden for two years and the disease was in an advanced stage with osteoporosis and destruction of the cartilage, but there were no signs of activity. In the other cases there was some improvement in joint movement as well, the greatest degree of improvement being noted in cases in which there were signs of activity of the disease. Two cases of Still's disease, one in a child 4½ years of age, and the other in a young man of 17 showed very definite improvement. In the latter case treatment was begun during a febrile period, and almost complete remission was obtained. In 3 cases in which there was a recurrence, 1 was relieved by a course of progesterone. In another, definite improvement followed the administration of ACTH and was maintained by the subsequent use of progesterone;

in another case, however, in which the recurrence developed almost immediately after the cortisone treatment was stopped, ACTH had no favorable effect but rather seemed to aggravate the symptoms. From these observations the authors conclude that immediately after a course of cortisone therapy the adrenal cortex does not respond to stimulation by ACTH, but after a certain interval (in their case, one month) ACTH is effective. In the 2 cases of Still's disease, improvement has been maintained. The child with Still's disease was given one course of gold salt therapy; and the other patient with Still's disease is still receiving cortisone in a dosage of 200 mg. weekly in two divided doses.

In spite of the fact that large doses of cortisone were used (2 of the patients being given as much as 5 Gm.), no harmful hormonal effect was noted, no rise in blood pressure (except in 1 patient in whom blood pressure was low), no edema, and no case of "moon-face." In some cases there was considerable insomnia during the treatments. On the basis of these observations, the authors come to the conclusion, that cortisone is indicated especially in active stages—acute or subacute—of polyarthritis; in the late stages, when activity has subsided, it is of comparatively little value, except for the relief of pain. As long as the supply of cortisone is limited, it should be used in the active stages of the disease, including exacerbations in which there are signs of involvement of joints not previously involved. As the conditions of the joints improve, physiotherapeutic and orthopedic procedures should be employed as indicated to increase the range of movement and maintain correct attitudes.

Treatment of Disorders of the Thyroid Gland with Radioactive Iodine. SIGVARD KANE, AND OLAF PETERSEN, Copenhagen, Denmark. Ugesk. f. laeger. *113*:253-57, March 1, 1951.

Twenty-six patients with cancer of the thyroid gland were studied with reference to treatment with radioactive iodine, I^{131}. In only 6 of them (4 with raised and 2 with normal basal metabolism) was it possible to administer rather large doses for a considerable length of time. In 1 case there was objective disappearance of the tumor tissue and subjective improvement. In 2 cases the basal metabolism was reduced to normal levels and there was considerable subjective improvement. In 1 of them the improvement was only temporary, and in the other the observation period is only 7 months; in neither of these 2 cases was there objective disappearance of the tumor. The other cases showed neither objective nor subjective improvement.

The complications of the treatment were, apart from the intended hypothyroidism, severe edema of the larynx with fatal result in 1 case, beginning damage to the bone marrow (after a total dose of 576 mC I^{131}) in 1 case, and transient swelling of the submaxillary salivary glands in 1 case.

The Nature of the Circulating Thyroid Hormone in Graves' Disease. I. N. ROSENBERG, Boston, Mass. J. Clin. Investigation *30*:1-10, Jan. 1951.

Studies were made of the plasma of 6 hyperthyroid patients who had received therapeutic doses (10-15 mc.) of radioactive iodine (I^{131}) 2 to 10 days previously. The

plasma proteins were precipitated by trichloro-acetic acid, and washed; 97 to 99 per cent of the plasma I^{131} was found to be protein-bound. Approximately 95 per cent of the labelled precipitable iodine could be readily extracted by n-butanol. Characterization of the I^{131} in the plasma butanol extracts was accomplished by filter paper partition chromatography with and without added amino acids (thyroxine, diiodotyrosine, monoiodotyrosine, and acetylthyroxine) using the solvent systems n-butanol:glacial acetic acid:water (75:10:15) and n-pentanol: pyridine:water (40:40:15). The location of the labelled iodine on the developed chromatograms was established by measurement of radioactivity and was compared with the position of the known added amino acids. In each case, the I^{131} was found in only one position which corresponded well with that of thyroxine, and no radioactivity was found in spots corresponding to mono- and diiodotyrosine. When crystalline thyroxine was added to a butanol extract of plasma, and the mixture subjected to elution development on a cellulose column, practically all of the I^{131} emerged as a single band, and the effluent curves of concentration of thyroxine and of radioactivity were virtually superimposable. These results indicate that in Graves' disease the circulating thyroid hormone is indistinguishable from thyroxine. Since it is well known that the serum protein-bound iodine may be increased by the ingestion of organic iodine compounds and even of inorganic iodide, and since the circulating thyroid hormone appears to be thyroxine, the functional state of the thyroid gland may be reflected more closely in the concentration of plasma thyroxine than in the protein-bound iodine. 35 references. 2 figures. 1 table.—*Author's abstract.*

First Results of Hormone Treatment of Rheumatic Polyarthritis (Still's Disease). (Premiers résultats un traitement hormonal de la polyarthrite rhumatismale (maladie de Still)). LAMBERT, TAGNON, AND WATTHEZ. Acta paediat. belg. 5:58-64, No. 1, 1951.

A case of Still's disease in a girl 10 years of age who had been bedridden for several months was treated first with ACTH in a dosage of 15 mg. daily given in four injections at six hour intervals for seven days. The patient was able to walk alone 48 hours after treatment was begun and showed progressive improvement. The ACTH treatment was followed by treatment with insulin given daily in doses sufficient to produce hypoglycemia for 17 days. The improvement induced by ACTH was well maintained, except that at the end of the period of insulin treatment there was a slight increase in the swelling of the joints of the hands and of the wrists and knees, but little, if any, loss of motility of the joints. Cortisone in a dosage of 30 mg. daily and pregnenolone in a dosage of 100 daily were then given for 20 days. When the child was discharged from the hospital she was able to move easily and play with other children; her gait was normal after correction of luxation of the right hip. A follow-up examination two months later showed that the swelling of the joints had increased again, and movement of the joints was sometimes painful, but the range of motion was good. Another course of treatment with cortisone and pregnenolone for 15 days relieved all pain in the joints and increased the range of motion slightly. The sedimentation rate, which had been reduced by the earlier course of treatment, remained low.

Observations on a Case of Idiopathic Hypoparathyroidism. ARTHUR JORDAN, AND A. R. KELSALL, Sheffield, England. Arch. Int. Med. *87*:242-58, Feb. 1951.

A case is described, showing the classical features of idiopathic hypoparathyroidism. The patient, a boy of 17 years, had chronic tetany of at least eight years duration, a persistently low serum calcium and high serum inorganic phosphate, normal renal function, and no steatorrhea; his diet was normal, and he had had no operation on the neck. The patient showed continual muscle twitching and gave a history of epileptiform attacks. He was of small stature, with hair of somewhat feminine distribution, and only nine erupted teeth. Chvostek's sign was positive, and voluntary hyperpnea precipitated tetany. Early cataracts developed while he was under observation. X-ray examination showed many unerupted teeth, some sclerosis of the diaphyses of the long bones, and bilateral mottled calcification of the frontal areas of the brain, perhaps associated with the choroid plexus. Laboratory findings were normal apart from the low serum calcium (6.3 mg./100ml.), the raised inorganic phosphate (9.1 mg.P/100 ml.), and a serum alkaline phosphatase of 33 King-Armstrong units. An injection of parathyroid hormone produced a rise in serum calcium and a fall in serum inorganic phosphate.

A balance experiment showed that the intake of calcium and magnesium was slightly greater than the excretion, the difference being of doubtful significance; the loss of phosphorus exceeded the intake by 342 mg. daily. The electrocardiogram showed no gross changes but the Q-T interval was at the extreme upper limit of normality. Treatment with calcium lactate powders alone and combined with large doses of calciferol was without effect. A high protein diet combined with calcium lactate and calciferol led to an immediate response, the tetany ceasing, and the serum calcium and inorganic phosphate levels returning to normal. Treatment with calcium and calciferol was continued; no relapse occurred, although the high protein diet was discontinued. There was some regression of the lens opacities.

The literature of idiopathic hypoparathyroidism is reviewed briefly, and the relationship of the neurologic manifestations, of intracerebral calcification, and of ectodermal lesions to hypoparathyroidism is discussed. 45 references. 7 figures. 3 tables.—*Author's abstract.*

The Use of Antithyroid Drugs. D. W. PETIT, Los Angeles, Calif. California Med. *74*:99-104, Feb. 1951.

The following types of problems should be handled with anti-thyroid drugs: (1) preoperatively for (a) young patients with uncomplicated hyperthyroidism, (b) hyperthyroid patients with cosmetic or mechanical defects from an enlarged thyroid, and (c) patients with hyperthyroidism and possible malignancy of the thyroid; (2) as a temporary control of hyperthyroidism during pregnancy; and (3) the occasional remaining patient with hyperthyroidism who, for individual reasons, is not suitable for surgery or radioactive iodine therapy.

The preparation of a patient with complicated hyperthyroidism for thyroidectomy may require six months to a year. Such patients should be prepared for whatever length of time it takes to render them not only euthyroid but also rehabilitated.

The long term use of antithyroid drugs is less effective for the "cure" of hyperthyroidism than surgery or the use of radioactive iodine.

Propyl and methyl thiouracil are the available antithyroid drugs of choice. Both of these thiouracil derivatives are capable of producing leukopenia. Dose schedules for these drugs are outlined. The antithyroid drugs exert no favorable effect on exophthalmos. The antithyroid drugs are suitable for the control of hyperthyroidism during pregnancy. The patient probably should not be kept hypothyroid during pregnancy but rather in a state of mild hyperthyroidism. 27 references. 1 chart. 5 tables.—*Author's abstract.*

The Celiac Syndrome with Adolescent Rickets. R. WILSON, Ireland. Irish J. M. Sc. *6*:39-42, Jan. 1951.

The patient has been under constant medical supervision since the earliest days of his life, and the records of his progress are reasonably complete. He came under our care in 1946, aged 18 years, suffering from severe rickets and celiac disease with stunted growth. Examination of the records has failed completely to expose any evidence of his having suffered from symptoms of acute rickets prior to 1942. The factors necessary for the production of rickets were present ever since the child first produced his typical fatty stools at the age of 18 months. The reason the patient did not develop rickets lies in the associated retardation of growth which is found in celiac disease. The bones must be growing actively to expose the existence of rickets. Rickets were present all along in a latent form in this child; but, as bone growth was so retarded, the rickets did not show itself. When he reached 14 years, growth began to take place actively and then rickets flared up. The acuteness of the rickets is in a large measure proportional to the rate of bone growth. The institution of treatment, which consisted of a high protein, low carbohydrate and low fat diet, together with intensive dosage with Vitamin D (Sterogyl) and calcium, was immediately followed by clinical improvement. The blood changes were much less dramatic: this was especially marked in the case of the blood calcium. It took nine months to raise the calcium level to approximately normal. The alkaline phosphatase, on the other hand, would appear to be a much more sensitive indicator of progress, as it showed an immediate rise, followed by a gradual but persistent fall. Improvement was shown in the absence of any marked change in the faeces. 5 references. 4 figures.—*Author's abstract.*

NERVOUS AND MUSCULAR DISORDERS AND DISEASES

Hysterical Abdominal Proptosis. N. J. ROUSSAK, Manchester, England. Gastroenterology *17*:133-37, Feb. 1951.

Patients of either sex complain frequently of abdominal distension, lasting minutes, hours, or even months, which subsides without passing flatus or eructating. When these patients are examined the whole abdomen may appear to be grossly distended, or only a part of it, and "phantom tumors" are sometimes felt. The apparent distension always subsides at once, without the passing of gas, when anesthesia is induced, but usually recurs as anesthesia wears off. Roentgenograms do not show excess intestinal gas.

One of the 5 patients described here could voluntarily produce the distension after it had ceased to occur spontaneously; roentgenograms showed that the diaphragm dropped about 3 inches when the abdomen protruded and continued to move normally at this lower level. The diaphragm of another patient rose considerably, simultaneously with induction of anesthesia and subsidence of the distension.

The mechanism by which the distension is produced seems to be the raising of the intra-abdominal pressure by descent of the diaphragm, combined with localized or generalized relaxation of the abdominal muscles.

All of these patients are highly strung, and some have had other hysterical complaints. 6 references. 3 figures.—*Author's abstract.*

Role of Birth Injury and Asphyxia in Idiopathic Epilepsy. J. M. NEILSEN, AND C. B. COURVILLE, Los Angeles, Calif. Neurology, *1*:48-52, Jan.-Feb. 1951.

There is a strong evidence from both the clinical and pathologic viewpoints that idiopathic epilepsy is due to small cortical focal areas of damage in individuals with lowered convulsive thresholds. Firstborn children, because of difficulties during birth, are twice as susceptible to epilepsy as are children subsequently born to the same mother. Children of subsequent birth may suffer from exactly the same difficulties at birth as do the firstborn, and consequently they may also have epilepsy due to birth trauma or asphyxia. The focal lesion resulting from asphyxia or birth trauma acts as a trigger mechanism but is not adequate to produce epilepsy in all persons. A lowered convulsive threshold, as indicated by cerebral dysrhythmia, is necessary in many instances. Estimates indicate that 40 per cent of all cases of idiopathic epilepsy are in firstborn children. A small per cent of those subsequently born also develop epilepsy because of birth trauma. Probably more than one half of all cases of essential epilepsy are the result of birth injury asphyxia. The remainder are due to a variety of causes of cerebral damage. In the conviction that there is a cerebral focal lesion mechanism in each case of idiopathic epilepsy, the authors believe that each case should be evaluated from the standpoint of surgical intervention. Even though surgical intervention may be successful only in a minority of cases, it should be considered.

Neurocirculatory Asthenia: Diagnosis and Treatment. N. E. REICH, Brooklyn, N. Y. Am. Pract. *2*:120-23, Feb. 1951.

In spite of the confusion in terminology and etiology which attends this condition, the correct diagnosis and proper treatment are important in view of its marked prevalence, especially in times of stress. It is doubtful whether any specialty in medicine has completely escaped contact with this condition because of the great variety and inconstancy of symptoms. Although there are evidences of cardiovascular, respiratory, and peripheral neurogenic dysfunctions, the first of these usually dominates the clinical picture. For example, more than half the patients with cardiac complaints suffer from an unnecessary anxiety about their hearts arising from suggestion.

Symptoms are multiple, unrelated and include fatigue, exhaustion, nervous lability, palpitation, breathlessness (sighing or panting), irritability, apprehensiveness, in-

somnia, inability to perform heavy work or concentrate, left thoracic pain (usually localized at nipple, left cardiac border or left axilla), unhappiness, nightmares, flushes, sweating, and giddiness. Precordial pain occurs in more than half the cases and is described as aching, soreness or "twinge", usually sharply localized and never entirely substernal. There may be tenderness of the chest wall, but characteristic radiation of coronary pain is absent.

Signs are usually limited to tachycardia, tachypnea, unstable blood pressure, overactive heart action, and a quick but sometimes roughened first apical sound. Occasionally, a transient zero diastolic pressure is obtained in the brachial arteries, but it is normal in the lower extremities. Laboratory tests are based on the fact that such subjects show marked objective changes under stress. They include capillary microscopy, plethysmograms, pain reactivity, and psychologic tests, work tests, palmar sweat response, ventilation tests, cardiac output studies, and electrocardiograms. Treatment requires skill, tact, and thorough examination on the part of the physician. Graduated exercise and reassurance is the keynote of treatment. 4 references. 3 figures—*Author's abstract.*

Neural Mechanisms Involved in Itch, "Itchy Skin," and Tickle Sensations. D. T. GRAHAM, H. GOODELL, AND H. G. WOLFF, New York, N. Y. J. Clin. Investigation. *30*:37-49, Jan. 1951.

The sensation of itch has two subjectively distinguishable components, one pricking and the other burning. These correspond to the two kinds of cutaneous pain and are mediated respectively by the two types of nerve fibers involved in the transmission of pain from the skin. Touch receptors and fibers are not involved.

Cutaneous tickle and the sensation elicited in "itchy skin" do not differ qualitatively from itch, except by the addition of an awareness of movement, and are mediated by the same neural structures, i.e., those which transmit pain. Touch receptors, when functioning, probably add an essentially extraneous component to tickle and to the sensation elicited in "itchy skin," but both phenomena occur in the absence of touch.

When itching is present, the pain threshold at the site is lower than it is in the same skin during itch-free intervals. Itch occurs when pain receptors are weakly stimulated.

Tickle, itchy skin, and itch are abolished by pin pricks in adjacent skin. In the case of itch, this abolition is possible if the skin is pricked anywhere in the dermatome which contains the site of itching.

Tickle, "itchy skin," and itch do not occur in areas of secondary hyperalgesia. They do occur in skin surrounding sites of noxious stimulation when the area is hypoalgesic to pin prick.

It is suggested that the sensation of itch results from the presence in the spinal cord of impulses traveling in circuits of internuncial neurons, with a consequent patterned discharge up the spinothalamic tracts. Such circuits are presumably established when peripheral pain nerves discharge into the cord at a low frequency. When the circuits are broken up—by strong stimulation in the same dermatome, for instance—itching ceases. 28 references. 7 figures.—*Author's abstract.*

MISCELLANEOUS

Low-Back and Sciatic Pain. HENDRIK J. SVIEN, Rochester, Minn. Minnesota Med. *34*:57-58, Jan. 1951.

Tumors of the spinal cord, situated as high as the level of the tenth thoracic vertebra may mimic the syndrome of protruded lumbar intervertebral disk. The opinion is stressed that it is only by intraspinal investigation, that is, manometric and analytic studies of the spinal fluid and contrast myelography, not only of the lumbar region but of the lower half of the thoracic region as well, that the true nature of the lesion producing the "typical" syndrome of protruded lumbar intervertebral disk can be determined.

In a review of 1,296 consecutive cases of intraspinal operations from the level of the tenth thoracic vertebra down, it was noted that 1,242 operations were carried out for removal of protruded disks, and 51 operations were done for removal of tumors of the spinal cord. In the other 3 cases localized arachnoiditis was found.

Twenty-four of the 51 tumors of the spinal cord were evident on initial examination. In the remaining 27 instances, however, the working diagnosis, made after a study of the history and after general neurologic, orthopedic, and roentgenologic examinations, was "protruded lumbar intervertebral disk suspect." In all 27 cases, neurologic findings were minimal or absent, and roentgenologic survey showed only a narrowed interspace, slight scoliosis, or hypertrophic changes in some cases. Fifteen of the 27 tumors were situated above the level of the fourth lumbar interspace and would have been missed if only direct exploration of the fourth and fifth lumber interspaces were carried out, inasmuch as most of these tumors were intradural and presented no extradural manifestation.

The authors practice, and strongly recommend, routine intraspinal investigation in all cases in which protruded lumbar intervertebral disk is suspected regardless of how "typical" the symptoms may seem—*Author's abstract.*

The Use of the Wintrobe Hematocrit Tube in the Office Laboratory. J. W. KYLE, AND S. G. RICHMOND, Memphis, Tenn. J. Tennessee State M. A. *44*:51-55, Feb. 1951.

The use of the Wintrobe hematocrit tube in the routine examination of patients has the advantages of simplicity, economy, accuracy, and the wide variety of information obtained at a minimum of effort.

Wintrobe described several practical uses of his hematocrit tube. From the same cubic centimeter of blood, the following may be obtained: (1) the erythrocyte sedimentation rate: (2) the presence of anemia or polycythemia (packed volume of red-cells); (3) the presence of leukopenia, leukocytosis, or alteration in the quantity of blood platelets (packed layer of leukocytes and platelets); and (4) the appearance (color or opacity) of the blood plasma.

Features of special importance in the technic are the proper anticoagulant mixture of ammonium and potassium oxalate to prevent shrinkage of red cells and the use of a centrifuge capable of delivering 3000 R.P.M. to obtain the packed cell volume.

The erythrocyte sedimentation rate is a widely used test for the presence and intensity of certain diseases associated with tissue destruction. Abnormal sedimentation rates reflect changes in the plasma proteins caused by disease, but anemia (with the exception of sickle cell anemia) also increases the sedimentation rate. The question of the advisability of "correcting" the sedimentation rate for anemia is still unsettled.

In our experience with the sedimentation rate as a screening test for disease in 752 individuals, our favorite technic for screening was a modification of the Rourke-Ernstene method with correction for anemia and with 0.5 mm. per minute as the upper limit of normal. When some of the acute and dramatic diseases which cause an increased sedimentation rate are ruled out, the test may be used to advantage to detect occult disease such as cancer, chronic infections, or tuberculosis. Other well-known uses of the sedimentation rate are in differential diagnoses and to follow the degree of activity of certain disease processes. The hematocrit (packed volume of red cells) is the most accurate of the tests performed with the Wintrobe tube. Indeed, it is the most accurate and reproducible laboratory method for determining the presence and degree of anemia and polycythemia. In addition, the factors of skill and experience are of much less significance in performing this test as compared with red cell counts and hemoglobin determinations. The latter should not be done as a routine screening procedure but should be done for the proper classification of anemias discovered by the hematocrit.

The superficial layer of packed leukocytes and platelets is commonly called the buffy coat. Normally this layer varies from 0.5-1.0 mm. in thickness. The thickness of the buffy coat proved to be a reasonably good rough screening test for abnormal leukocyte counts in a group of 442 individuals. This is in accord with the work of Wintrobe. Leukocyte counts do not have to be done in routine screening but should be done if the count is important for differential diagnosis or if the thickness of the buffy coat is abnormal.

Jaundice or lipemia may be observed by simple inspection of the supernatant plasma.

The technic of using the Wintrobe tube in the routine examination of patients is especially recommended to the practitioner with limited office personnel and laboratory facilities or to the one who does no screening examinations on the blood. Indeed, we recommend that the tests performed with the Wintrobe tube, combined with examination of the stained blood smear, be substituted for routine red and white cell counts and hemoglobin determinations in offices and hospitals where those examinations are being done for screening. Blood cell counts and hemoglobin determinations would be done only when there were significant abnormalities in the hematocrit, buffy coat, or blood smear; for differential diagnosis; or in the typing of anemias. 3 references. 3 tables.—*Author's abstract.*

Studies with Labelled Anterior Pituitary Preparations: Adrenocorticotropin. MARTIN SONENBERG, New York, N. Y. Endocrinology *48*:148-61, Feb. 1951.

Anterior pituitary preparations with adrenocorticotropic activity were labeled by iodination with traces of radioactive iodine (I^{131}). These preparations, as well as control substances, inorganic iodide labeled with I^{131} and radio-iodinated bovine serum

albumin were injected intracardially to male rats. The animals were sacrificed at various periods of time, and the tissues were assayed for radioactivity by direct measurement and by radioautography.

After the administration of a radioactive ACTH preparation, radioactivity was found in significant concentrations in the adrenals, blood, liver, spleen, and later in the experiment in the thyroid. The concentration of radioactivity in the adrenals and other organs fell rapidly so that little radioactivity could be detected after four hours. The biological half life of this material in the adrenals was approximately 5.5 minutes. There was significantly less radioactivity in the adrenal after the administration of inorganic iodide labeled with I^{131} or radio-iodinated bovine serum albumin.

When iodinated ACTH was prepared with an iodine to protein molecular ratio of 2:1, there was still retention of biologic activity.

The radioautograph of the adrenal revealed considerably more exposure in the cortex with a definite preference for the inner layers. 23 references. 3 figures. 4 tables. —*Author's abstract.*

Uses and Abuses of the Clinical Laboratory. M. C. DARNELL, Lexington, Ky. J. Kentucky State M. A. *49*:55-60, Feb. 1951.

The author discusses the limits of accuracy of certain laboratory data and the limited inferences allowable from such data. The importance of screening tests is emphasized. An attempt is made to formulate a series of tests, the performance and interpretation of which should be helpful to the average physician in raising or confirming suspicion of the most common diseases. It is noted that in private practice the physician should not use precise, time-consuming, expensive tests in situations where less precise ones would yield the same information; that the performance of complicated tests should be entrusted only to experienced technicians; and that unless the results of such tests can be interpreted into corrective action the expense of their performance is unwarranted. 9 references. 2 tables.—*Author's abstract.*

The Current Status of the Electron Microscope in Thin Tissue Studies. E. F. GEEVER, R. F. DENT, JR., AND M. BARHITE, Colorado Springs, Colo. Rocky Mountain. M. J. *48*:99-101, Feb. 1951.

This is a preliminary report of an experience of 18 months with an RCA electron microscope in the field of direct thin tissue studies. The instrument used in this work is a small 30,000 volt console model. The technic used is that recommended by Newman, Borysko, and Swerdlow. Tissue preparation requires the highest technical skill, since the specimens must be sectioned less than 0.5 micron in thickness as electrons have very little penetrating power. The technic employed uses a lucite plastic medium which furnishes greater brittleness than paraffin and facilitates thinner sectioning. Furthermore, the unit of advance in the ordinary microtome is entirely too coarse and in this work a technic also recommended by Newman, Borysko, and Swerdlow is used wherein the tissue is frozen and then short intervals of thawing are permitted with thermal expansion advancing the specimen toward the knife in fractions of a micron.

The photographic problems are less formidable. The services of an electrical engineer are essential and in large cities where branches of RCA are maintained this problem is less serious than in smaller communities. Satisfactory progress has been made in this institution with a team which includes an electrical engineer, an histologic technician, and a pathologist. Examples of normal and cancer cells are illustrated at magnifications up to 5,000 x. The authors feel that the electron microscope will prove to be a valuable tool in the future in the field of direct tissue studies. 8 figures.—*Author's abstract.*

Arrhenoblastoma. P. F. ECKMAN, Duluth, Minn. Minnesota Med. *34*:152-54, 89, Feb. 1951.

The author reviews the incidence, theories of origin, and clinical features of the interesting and relatively rare neoplasm—arrhenoblastoma—as found in the available literature.

The case history of a young woman (born 1921) who had an arrhenoblastoma is added to the literature by the author. In this case there was an unusual sequence in which a pregnancy was thought to have originated during a period of spontaneous remission of functional activity of the tumor, prior to its recognition and surgical removal. In addition, two normal pregnancies occurred subsequent to operation.

The patient, an apparently normal young woman, first evidenced the functional effect of this tumor in the spring of 1941; at this time she also had nervous symptoms, flushes, palpitation, and weakness. Amenorrhea began in June of 1941 and, although it persisted, she married in July of 1942. She manifested some interesting defeminizing and masculinizing physical changes, such as a gain in weight, breast atrophy, change in hair distribution, marked hypertrophy of the clitoris, and increased libido. Menstruation was spontaneously re-established in July of 1943 and in December of 1943 was followed by the inception of pregnancy. An ovarian tumor was first recognized on postpartum examination and subsequently removed surgically.

Since removal of the arrhenoblastoma, the patient has had two additional normal pregnancies. She has remained well and free of recurrence. 13 references. 4 figures. —*Author's abstract.*

The Inhibition of Gonadotrophic Hormone Secretion by Physiological Doses of Estrogen. WILLIAM W. BYRNES, Madison, Wisconsin. Endocrinology *48*:133-36, Feb. 1951.

When two natural estrogens, alpha-estradiol and estrone, and one synthetic estrogen, 3-(p-hydroxyphenyl)-4-(p-acetylphenyl) hexane, were injected into immature ovariectomized rats in parabiosis with intact females, the gonadotrophic hormone (F. S. H.) was inhibited by the hormones at levels below those causing uterine stimulation. It is suggested that in intact, immature female rats, gonadotrophic secretion is inhibited by estrogen at very low and physiologic levels.

Although the trauma inherent in the parabiosis procedure was found to cause some ovarian atrophy, this was more than compensated for by the hypersecretion of gonadotropin when one rat was ovariectomized. 9 references. 1 table.—*Author's abstract.*

dermatology

Quinidine-Induced Exfoliative Dermatitis. D. R. TAYLOR, AND R. POTASHNICK, St. Louis, Mo. J.A.M.A. *145*:641-42, March 3, 1951.

The authors report a full-blown case of exfoliative dermatitis with transient hepatitis and generalized lymphadenopathy occurring in a 59 year old white male who had been receiving quinidine sulfate for two months for control of paroxysmal supraventricular tachycardia.

The clearing of the dermatitis and improvement in liver function values on each of two occasions when quinidine was withdrawn and the prompt recurrence of exfoliation when quinidine therapy was reinstituted strongly suggested that this reaction represented an idiosyncrasy to quinidine.

A search of the literature failed to uncover a previous report of exfoliative dermatitis induced by quinidine.

Other quinidine idiosyncrasies of a serious nature were reviewed and included: transient respiratory arrest, acute delirium, thrombocytopenic purpura, eczematoid skin eruptions, a scarlatiniform rash, sinus thrombosis, and recurrent fever accompanied by transient splenomegaly and leukopenia. 9 references.—*Author's abstract.*

Treatment of Eczematous Dermatoses. The Topical Use of an Antihistamine Agent Combined with Chloroiodohydroxyquinoline. ALEX S. FRIEDLAENDER, Detroit, Mich. J. Michigan M. Soc. *50*:54-56, Jan. 1951.

This report deals with the combined topical use of two valuable agents in the treatment of eczematous skin eruptions. The effectiveness of chloroiodohydroxyquinoline and pyranisamine maleate, an antihistaminic drug, combined in a bland, nongreasy vehicle, has been striking enough to warrant a summary of the results observed in cases of atopic dermatitis, contact dermatitis, and other eczematous eruptions. Chloroiodohydroxyquinoline in 2 or 3 per cent concentrations exhibits bacteriostatic and fungustatic properties and has been widely used in the local treatment of atopic, contact, and seborrheic dermatoses, sycosis barbae, stasis dermatitis, bacterial and mycotic infections of the skin, pruritus ani and vulvae, and psoriasis. Its low sensitization index and relatively nonirritating qualities have given it a position high on the list of effective dermatologic agents. Pyranisamine maleate, which is dimethylaminoethylmethoxybenzylaminopyridine, is an unusually strong antagonist of histamine and ranks high among the available antihistamine preparations in point of therapeutic effectiveness, both in the case of oral administrtaion and topical application. Our own experience has shown that a 2 per cent preparation in a water-miscible cream exerts a high degree of antipruritic action with a minimum of irritation when applied to acute, subacute, and chronic eczematous eruptions. The base used to incorporate the active ingredients under study consisted of a water-washable ethylene glycol stearate dispersion in methoxycellulose gel which in itself appears to exert an emollient action.

Fifty-seven patients in the following categories were treated with the combination cream:

Condition Treated	No. of Patients	Improved	Not Improved	Aggravated
Atopic dermatitis				
Adults and older children	32	31	1	0
Infants	9	7	2	0
Contact dermatitis	9	7	0	2
Infectious eczematoid dermatitis	3	3	0	0
Stasis dermatitis	2	2	0	0
Dermatitis herpetiformis	1	0	0	1
Nummular eczema	1	1	0	0
Total	57	51	3	3

Because of the many factors involved in atopic dermatitis, contact dermatitis, and the other eczematous eruptions discussed, it cannot be anticipated that topical therapy alone will cure these conditions. Excellent results are frequently obtained in these situations by careful allergic investigation, with subsequent control of the specific sensitizations responsible for the dermatitis. Local therapy, however, is often necessary to control pruritus and may help to induce a remission. Both pyranisamine maleate, 2 per cent, and chloroiodohydroxyquinoline, 3 per cent, as well as the emollient base in which they were combined, are bland and relatively nonirritating substances, even when used in acutely inflamed skin. Many of the patients in this series who have used a great variety of local medicaments during the period of their difficulty, in some instances extending over a period of years, remarked that the combination cream was the most satisfactory preparation they had yet encountered. 8 references. 1 table.—*Author's abstract.*

Dermatomyositis with Vesicular and Bullous Lesions. G. H. FINDLAY, E. A. PRICE, AND C. R. J. VAN RENSBURG, Pretoria, South Africa. South African M. J. 25:60-65, Jan. 27, 1951.

Three cases of dermatomyositis are described in which vesicles and bullae were the predominant dermatologic manifestations. The first was a Negro female of 40 years who had had dermatomyositis, with muscle contractures, for three years. Vesicles, hypertrichosis, and pigmentation were noted on the exposed parts, and the trunk showed numerous small scars where vesicles had erupted previously. The second case was that of a 25 year old Negro with acute dermatomyositis which was fatal within four weeks. Bullae resembling those of acute pemphigus or Stevens-Johnson syndrome were present on pressure points, flexures, and in relation to orifices. The third patient, a Negro male of 20, had an acute dermatomyositis from which he recovered. A single large bulla appeared on one side of his neck.

Since publication a fourth case of dermatomyositis has been reported in a Negro male of 39 years in which bullae were present in the first attack, and the more typical erythematous and pigmentary changes without bullae in a relapse. 19 references. 4 figures.—*Author's abstract.*

Antibiotics in Dermatology. J. L. MILLER, M. H. SLATKIN, AND C. S. LINGAMFELTER, New York, N. Y. M. Clin. North America *35*:341-54, March 1951.

The authors, in reporting their findings on the use of antibiotics in the treatment of skin infections, stress the need for determining the sensitivity of the organisms present to various antibiotics and point out that the use of antibiotics in combination is often advisable.

Studies in the topical use of the antibiotics have shown that the sulfonamides, penicillin, bacitracin, and dihydrostreptomycin have all proved effective in the treatment of primary pyogenic infections as well as secondarily infected dermatoses, while preliminary studies with terramycin now in progress indicate that it, too, may be an effective agent. Because of the high percentage of sensitization, the use of the sulfonamides for local therapy is not advised. The use of penicillin ointment for five or six days seems justified (sensitization occurring about the eighth day), though preference should be given bacitracin or dihydrostreptomycin ointment. Bacitracin, with a low percentage of sensitization, was found to be worthy of trial in all cases of pyogenic infection of the skin. Aureomycin ointment is a valuable remedy, having proved successful after the failure of other antibiotic salves. Dihydrostreptomycin is valuable for usage over a short period; drug-fastness develops in less than two weeks.

The current tendency is to use the sulfonamides and penicillin less and less because of their fairly high sensitization rate, and in the latter case because resistance developed by organisms, particularly *staphylococci*, to penicillin is a factor of increasing importance.

The authors also discuss briefly the relative merits of each antibiotic in the diseases particularly amenable to such therapy. 48 references. 3 figures.—*Author's abstract.*

Treatment of the Pyogenic Dermatoses. RAY J. NOOJIN, Birmingham, Ala. J. M. A. Alabama *20*:277-83, Feb. 1951.

Two organisms, the hemolytic *Staphylococcus aureus* and the beta hemolytic *streptococcus*, are largely responsible for the pyodermata which in turn comprise a considerable portion of present-day dermatologic practice. The treatment of these cutaneous infections may become difficult if the organism is not sensitive to the drugs available, if the patient's own defenses are poor, or if other complicating factors occur.

The topical use of penicillin, the sulfonamides, furacin, and other drugs carries with it decided risks because of the danger of cutaneous sensitization. Therefore, what not to do is an important consideration.

With the large scale use of sulfonamides and penicillin, numerous serious limitations and reactions are appearing more frequently. It seems best to avoid the use of those drugs in the treatment of the pyodermata which may be needed urgently for other more serious diseases later.

At the present time penicillin is one of the most useful agents against the majority of these infections. However, there seems to be both an increase in the number of penicillin-resistant infections and also the number of patients who have become sensitized to the drug. The therapeutic advantages of penicillin may continue to decrease in the years to come because of these tendencies.

The important factors in the treatment of the pyodermata involve local debridement and the finding of a medicament to which the patient's organisms are sensitive. Overtreatment is often the cause of therapeutic failure. It is important that the physician become adept in the effective use of a small number of the least sensitizing drugs. This should prove more successful than trying to master a lengthy list of drugs whose skillful use will require considerable experience. 16 references.—*Author's abstract.*

Seborrheic and Senile Keratoses. M. R. CARO, AND F. J. SZYMANSKI, Chicago, Ill. M. Clin. North America *35*:419-31, March 1951.

Seborrheic keratoses and senile keratoses are distinct entities which differ from each other on the basis of clinical features, histopathologic findings, and prognosis.

Seborrheic keratoses are benign epidermal neoplasms, often pigmented, generally multiple, and, in most instances, covered by a scale that is greasy and shows follicular plugging. They do not tend to become malignant. Seborrheic keratoses are probably delayed epithelial nevi and may represent cutaneous ornaments similar to those seen in lower animals. For patients who do not consider them ornamental, many forms of effective treatment including curettage, electrosurgery, surgical excision, and the use of solid carbon dioxide, or local escharotics are available.

Senile keratoses develop as part of the aging process of the skin. They are observed most often on the uncovered parts of fair-skinned individuals who have been exposed excessively to the sun. Senile keratoses are precancerous lesions, and they should be destroyed completely. The selection of the method of treatment is guided by the clinical features of the lesion and the condition of the patient, but in all cases some form of mechanical removal of the keratosis is to be preferred. Care should be exercised to protect the skin in these patients from further exposure to the sun or to other local irritants.

The official designations of seborrheic keratosis and senile keratosis should be retained. 4 references. 8 figures.—*Author's abstract.*

Effects of Cortisone on Acute Disseminated Lupus Erythematosus. LOUIS A. BRUNSTING, Rochester, Minn. Arch. Dermat. & Syph. *63*:29-52, Jan. 1951.

The results of the administration of cortisone (and, in one case, ACTH also) were noted in 7 female patients with acute disseminated lupus erythematosus.

Cortisone acetate was administered by intramuscular injection in doses of 300 mg. the first day, then 200 mg. daily until symptoms were under control, and then 100 mg. daily for varying periods. One patient received the hormone for 166 days. Other patients received from 2 to 4 courses; the length of each course and the interval between courses varied with the symptomatic response of the patient or the development of untoward side effects.

With adequate doses of cortisone there was a dramatic response in each case. The fever subsided, stiffness and joint pains disappeared, the facial erythema subsided, and there was an improved sense of well-being and a gain in appetite. Pleural and pericardial friction rubs and signs of peritoneal irritation also subsided. These benefits began

within 2 to 3 days and were often complete within 7 to 10 days. Unfortunately they were only temporary. Five of the 7 patients had a return of some symptoms within 7 to 21 days after cortisone was withdrawn; 1 remained symptom-free for 2 months before relapsing, and 1 was still in a relative state of remission 10 months after a protracted course of cortisone. Three patients died while under observation.

Response as measured by laboratory studies was less marked. The leukopenia was less pronounced, and occasionally eliminated. The rapid sedimentation rates were only slightly depressed; albuminuria and hematuria were unaffected, except temporarily in one instance. The increased serum globulin was reduced slightly in 1 case and more definitely in another case for a brief period. In other cases it was unaffected. The Hargraves phenomenon in the bone marrow, including the presence of the so-called "LE cell" was diminished in some cases but not entirely abolished in any.

Undesirable side effects were noted in several cases and in various ways. Accumulation of interstitial fluid with or without frank edema resulted from the retention of sodium. In the milder cases, restriction of sodium chloride in the diet corrected the difficulty, and in later cases, prevented it. At times diuretics were necessary. In 1 case with severe renal involvement, fluid retention became severe and uncontrollable, and death ensued. Potassium levels in the serum were at times lowered considerably, requiring the administration of potassium chloride by vein or orally. Nervous and mental symptoms were noted, ranging from mild mental stimulation or anxiety to a temporary psychosis in 1 case. Hypercortisonism as manifested by rounding of the face and by acne, hirsutism and striae distensae, was noted in a few cases—most marked in the one receiving the prolonged course of the hormone. When intercurrent infections developed, the usual symptoms, such as fever and inflammatory reactions, were suppressed. Infections encountered were: localized subcutaneous abscesses, septicemia, peritonitis, and pneumonia. The masking of symptoms tends to lead to a dangerous sense of false security and postponement of necessary therapy.

Caution must be maintained in the administration of cortisone and ACTH; they should be given only when laboratory facilities are available for strict control.

These hormones are not curative but have distinct value in controlling acute symptoms, particularly in cases in which irreversible systemic damage has not occurred. 10 references. 4 figures.—*Author's abstract.*

Actual Causes of Certain Occupational Dermatoses. JOSEPH V. KLAUDER, Philadelphia, Pa. Arch. Dermat. & Syph. *63*:1-23, Jan. 1951.

A report is made of an additional series of 1,412 cases of cutaneous diseases in patients who presented claims for compensation under the Pennsylvania law. The cases previously reported and those now reported total 3,709; 2,850 of the patients were male and 859 female. The diseases of 1,673 (percentage of incidence, 45.08) were diagnosed as occupational in origin and those of 2,036 as nonoccupational.

The actual causes of the occupational dermatoses of the 1,673 are classified in the following groups, with the percentage of incidence: primary irritants (acids, alkalis, and solvents (nonaqueous)), 28.6 per cent; trauma and accidental injury, 22.6 per cent; sensitizing substances, 13.6 per cent; wet work (water alone, soap and water, and

alkaline salt detergents), 13.1 per cent; cleansing agents applied to the skin, 10.7 per cent; petroleum products and other causes (hydrochlorinated hydrocarbons, vegetable oil, and dust) of folliculitis, 9.2 per cent; and physical and biologic agents, 2.2 per cent.

Nonaqueous solvents were the predominating causal irritants. The trauma and accidental injury group included all dermatoses (18 different diseases of the skin) that resulted directly or indirectly from accident or injury. Substances causing sensitization dermatitis are enumerated. Wet work and methods of hand cleansing are discussed as causes of occupational dermatoses. Substances causing occupational folliculitis are enumerated.

Burckhardt's test of the ability of the skin to neutralize alkali and his test of its sensitivity to alkali are discussed.

The pH of the hands of normal persons ranged from 4.5 to 6.5 and that of the sweat-bathed skin was lower. The increase in the pH of the hands after exposure to alkali and duration of such increase are in relation to the duration of continuous exposure, frequency of intermittent exposure and degree of alkalinity to which the skin is exposed. The most pronounced change of pH and duration of change were observed in 2 patients employed as pot and pan washers. It required about 20 hours after cessation of exposure to soap solution for the pH of their hands to attain the normal range. The role of the buffer action of sweat is discussed. The effect of buffer agents on the pH of the hands after exposure to alkaline solutions was studied.

Study was made of the pH of the following commercial detergents: seven nonsoap detergents advised for dermatitic hands, 103 hand cleansers for industrial workers, and 19 nonsoap detergents for kitchen and household purposes. Of the hand cleansers for industrial workers, 94 were alkaline and 57 were gritty powders which predominantly contained one or more of the alkaline salt detergents. 31 references. 9 figures. 2 tables. —*Author's abstract.*

Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone in Diseases of the Skin. A. BENSON CANNON, J. G. HOPKINS, G. C. ANDREWS, H. F. COLFER, P. GROSS, C. T. NELSON, AND C. M. HOWELL, JR., New York, N. Y. J.A.M.A. *145*:201-206, Jan. 27, 1951.

Pituitary adrenocorticotropic hormone (ACTH) and cortisone were employed in the treatment of 7 patients with pemphigus vulgaris, 2 with unclassified "pemphigoid" eruptions and 2 with epidermolysis bullosa of the congenital dystrophic type. Two of the 7 patients with pemphigus vulgaris died, but the remaining 5 were greatly improved both in their skin condition and in general health. All 5 patients required varying amounts of maintenance therapy with the corticosteroids to prevent relapse, and there is no evidence that these hormones influenced the basic causative factor in this disease.

Practically complete remission of symptoms was obtained in 2 cases of pemphigoid eruptions, but these patients also relapsed and required retreatment. The cases of epidermolysis bullosa were unaffected by the administration of large doses of the hormones. 4 references. 6 figures.—*Author's abstract.*

Keratoderma Palmaris et Plantaris Congenitalis. D. MACAULAY, Derby, England. Brit. M. J. *No. 4702*:334-36, Feb. 17, 1951.

A case of the diffuse form of this condition is reported in an infant. Investigation of the family revealed that the condition had been inherited for seven generations. Inheritance was direct from affected parent to approximately half the offspring, indicating that the mechanism of inheritance was by a simple dominant. The defect was not apparent at birth but became manifest in the first three months of life, and once established was permanent and resistant to treatment.

This is the second occasion on which inheritance of this condition through seven generations has been recorded, and the first time it has been reported in members of the white race. Reference is made to four other affected families encountered in the English Midlands, and it is suggested that the condition is commoner than reports would suggest. 6 references. 3 figures. 1 chart.—*Author's abstract.*

Dermatitis Herpetiformis: A Follow-up and Survey of Treatment. G. A. GRANT PETERKIN. Brit. J. Derm. *63*:1-7, Jan. 1951.

Of 105 patients with dermatitis herpetiformis, 64 were males and 41 females, while 21 of the patients were under 5 years of age. It appears that dermatitis herpetiformis in children is commoner in Scotland than in most countries. Of 42 patients who were interrogated, 16 were clinically cured; in 19 the disease was still highly active; and in 7 the eruption was still present but in such a mild form that the patient did not trouble to use any treatment.

In 3 typical cases investigated by R. H. A. Swain, there was no evidence that a filterable virus was present in the bulla fluid. Focal sepsis did not seem to play an important part, and the only evidence of endocrine imbalance was afforded by the history in 5 cases. Contrary to the usual expressed opinion, psychosomatic factors did not seem to play a part; none of the patients were debilitated or neurotic, and all were doing a full day's work. The effect of treatment was disappointing. Aureomycin was quite ineffective as were the antihistamines. Of 24 patients given arsenic, 7 had had no recurrence of the disease. No patient was cured by sulphapyridine, though 6 were able to keep the disease under control for long periods with minimal dosage. 16 references. 1 figure. 1 table.—*Author's abstract.*

Porokeratosis (Mibelli). H. HABER, AND A. PORTER. Brit. J. Dermat. *63*:28-32, Jan. 1951.

A case of porokeratosis (Mibelli) in a girl 10 years is described, in whom characteristic lesions extended throughout the length of the right arm and leg.

Histologic examination of a hyperkeratotic lesion showed that, in this instance, pathologic process began within a hair follicle and caused its destruction. This in turn provoked a foreign body granuloma.

The average vitamin A in the plasma was 86 i.u./100ml. 25,000 i.u. of vitamin A were given for three months without benefit. Thorium X (2000 e.s.u.) was painted over selected areas on 20 occasions with considerable improvement, but without producing cure. 14 references. 3 figures.—*Author's abstract.*

syphilology

Syphilis Among the Navaho Indians. CHARLES S. MCCAMMON, Fort Defiance, Ariz. J. Ven. Dis. Inform. *32*:28-33, Feb. 1951.

A study of the syphilis problem among the Navaho Indians, the largest and one of the most primitive tribes in this country, is presented. The study was made by utilizing mass blood test records, hospital records of the five Navaho hospitals, laboratory records, and records from the obstetric service of the Navaho Medical Center and mortality statistics. From this material it was felt that the prevalence of syphilis for the age group 20 years and over is between 70 per thousand and 100 per thousand. For the total Navaho population the incidence is probably less than 55 per thousand. 10 references. 1 figure. 3 tables.—*Author's abstract.*

Treatment of Acute Gonorrhea in Men with Dihydrostreptomycin (Traitement de la gonococcie aiguë chez l'homme par la dihydrostreptomycine). A. S. NAHON, AND P. J. VIALA, Paris, France. Presse méd. *59*:104, Jan. 27, 1951.

Acute gonorrhea in men was treated by a single intramuscular injection of dihydrostreptomycin, 0.50 Gm., without the use of any retarding vehicle. Of the 228 patients treated, 80 per cent (178 patients) showed no discharge on the day following treatment. The urine was clear, except for a few filaments in the first glass, and all symptoms were relieved. In 18 per cent some dysuria with a slight discharge persisted for about 24 hours; the discharge contained many polymorphonuclear leukocytes, but no micro-organisms; in 2 per cent the discharge persisted for several days, but no gonococci were found. Other micro-organisms were present, which were not sensitive to streptomycin; this infection was cleared up with local treatments with antiseptics. Follow-up tests showed no recurrence of gonococcal infection. Streptomycin gave better results in the treatment of acute gonorrhea in men than has been obtained with penicillin. Streptomycin has no effect on the *Treponema pallidum* and thus does not mask an associated syphilitic infection as penicillin often does. With the dosage employed there were no reactions such as are observed with larger dosage and long-continued treatment.

Massive Doses of Amphetamine as an Adjuvant in the Treatment of Barbiturate Intoxication. HARRIS A. FRIEDMAN, Milwaukee, Wis. Am. J. M. Sc. *221*:133-36, Feb. 1951.

Nine cases sufficiently intoxicated by barbiturates to be comatose were treated in this series. In addition to intranasal oxygen, gastric lavage, and other symptomatic treatment as indicated, all patients were given massive doses of amphetamine. Ten to 20 mg. of dexedrine were administered intravenously and repeated as often as necessary—sometimes every five minutes. As respiration and blood pressure improved, the drug was given intramuscularly in reduced quantities and/or at longer intervals. Medication was usually continued until the patient responded to verbal stimuli. The quantity of dexedrine administered to these patients ranged from 160 mg. in five hours to 2,090 mg. in 25 hours.

The author's experience was entirely satisfactory. Undesirable side effects such as convulsions were not encountered. Complications which did occur were pulmonary. Eight patients recovered and one expired of acute pulmonary edema, 36 hours after admission. 8 references. 1 table.—*Author's abstract.*

Cryoglobulinaemia in Multiple Myelomatosis. A. N. BLADES, Brighton, England. Brit. M. J. *4699*:169-71, Jan. 27, 1951.

The author describes a case of multiple myelomatosis in which diagnosis followed upon the accidental observation that the serum solidified on cooling. The phenomenon was reversible on warming and could be repeated indefinitely. The effect is attributed to a high serum globulin. Twelve previous cases are described, and the clinical findings and diseases, with which the phenomenon is associated, are reviewed. In the case described, the greater part of the raised globulin was found in the gamma fraction; in other cases reviewed, in other fractions. Reference is made to the form of crystals in the serum and other cases and also to crystals found in plasma cells and kidneys. 20 references. 1 table.—*Author's abstract.*

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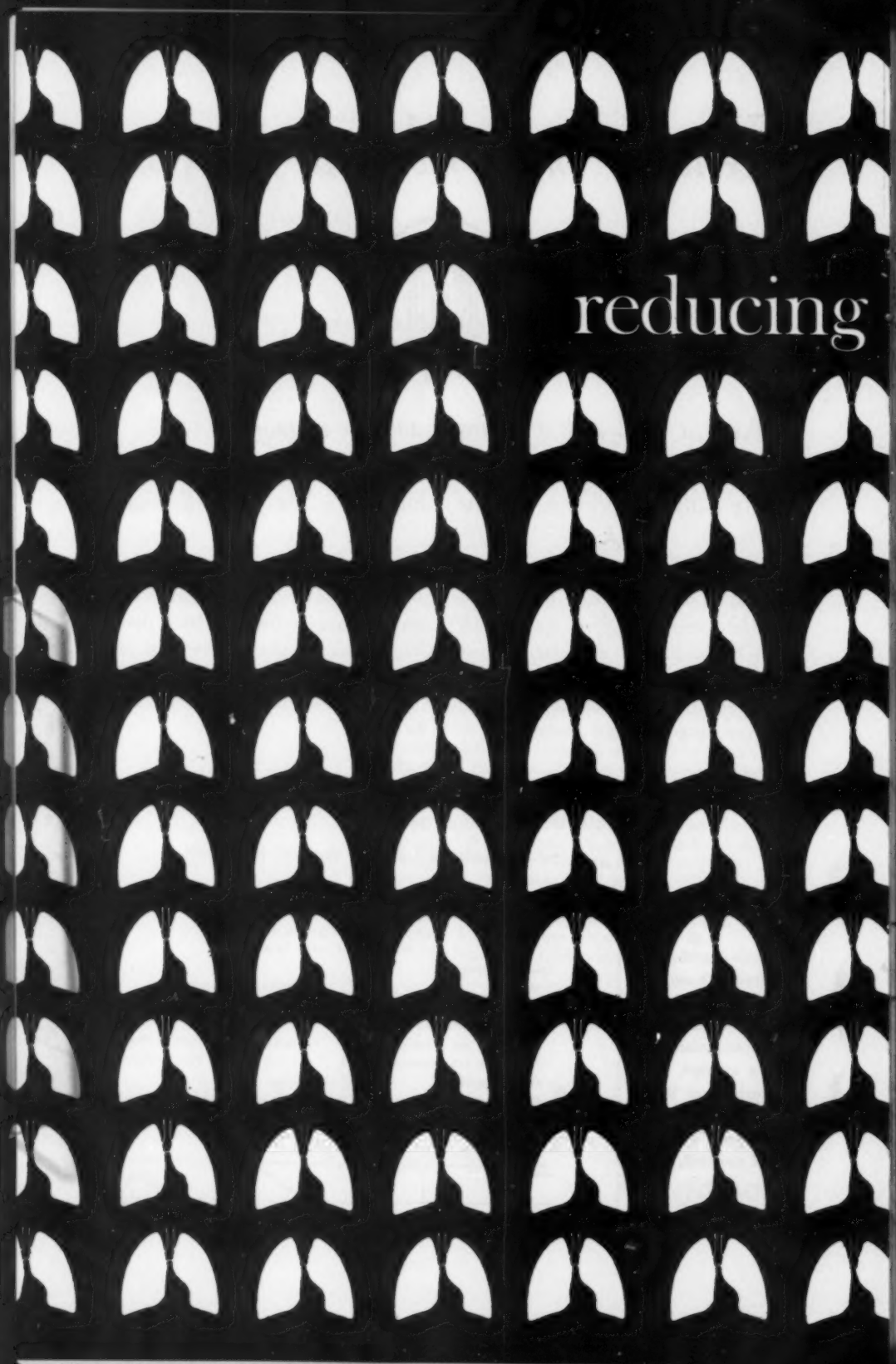
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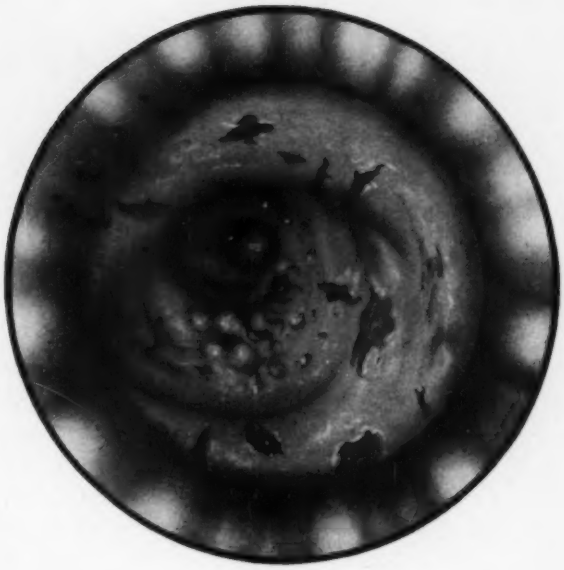

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1. *Dowling, H. F., et al.: Ann. New York Acad. Sc. 53:433 (Sept. 15) 1950.*

2. *Sayer, R. J., et al.: Am. J. M. Sc. 221:256 (March) 1951.*

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